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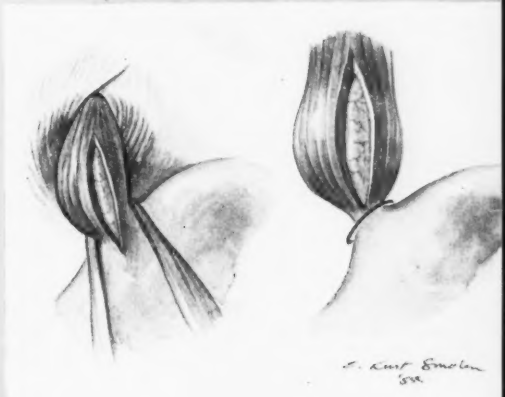

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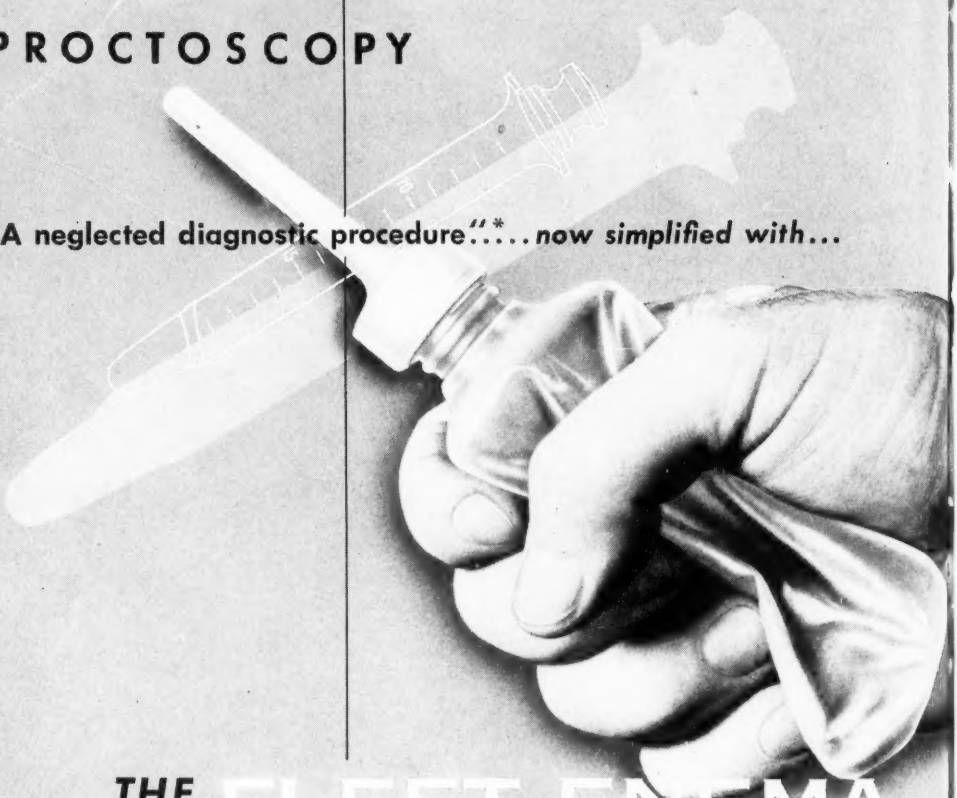

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A.M.A. Archives OF SURGERY

Unusual Manifestations of Parathyroid Adenoma

C. MARSHALL LEE Jr., M.D., Cincinnati
WILLIAM T. McELHINNEY, M.D., Covington, Ky.
and
EDWARD A. GALL, M.D., Cincinnati

Although the clinical manifestations and pathological physiology of hyperparathyroidism are now quite well recognized and understood, the diagnosis is still frequently overlooked until the opportunity for cure has been lost. This impression is borne out by the fact that when we recently surveyed the diagnostic files of seven general hospitals in a service area embracing about 1,500,000 persons over a 15-year period, only 11 proved cases of parathyroid adenoma were found. Nine of these cases are from hospitals with which we are directly connected, and only two were collected from other sources.

Among the 11 cases 4 were discovered at autopsy and in 7 the clinical diagnosis was made during life and confirmed at operation. Only 1 of the 11 cases was recognized in connection with urinary calculus as the presenting symptom. In another case a nephrectomy had been done for a large ureteral stone with septic destruction of the kidney, but no tests for parathyroid dysfunction had been done and the adenoma was found at autopsy, more than five months later. In two others urinary calculi were found after the diagnosis had been made.

Such a distribution in so small a series of cases suggests that diagnostic alertness and accuracy with respect to hyperparathyroidism might be substantially improved.

While the foregoing observations are recorded in the hope of encouraging livelier clinical interest in parathyroid disease, such a limited series does not alone deserve a special report. Four of the cases, however, are sufficiently unusual to merit documentation. These four cases will be recorded and commented upon in detail. The essential features of the 11 cases in the series as a whole are simply summarized in the Table as contributary to subsequent discussion.

REPORT OF CASES

Case 6.—This man was first admitted to the hospital Dec. 8, 1937, at age 18. Evaluation for renal disease was conducted after discovery of albuminuria at a routine school examination. He was discharged with a diagnosis of "chronic nephritis" and was not seen again for more than 10 years. He was admitted for the second time in July, 1948, with a history of progressively increasing weakness over the preceding eight years. One year prior to this admission he developed symptoms of peptic ulcer and two months later had a series of severe hemorrhages, requiring 17 blood transfusions. Three months prior to admission he was treated ineffectively for "bursitis" in the right shoulder.

His presenting complaint was of such severe weakness that he could not rise from a seated position without using his arms. He had lost 25 to 30 lb. in weight in a year. He was readmitted

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Read in part before the Central Surgical Association, Chicago, Feb. 18, 1955.

From the Departments of Surgery and Pathology, University of Cincinnati College of Medicine and the Cincinnati General Hospital, Cincinnati.

SUMMARY OF FINDINGS IN ELEVEN CASES OF PARATHYROID ADENOMA

Case No.	Race Sex & Age	Duration of Symptoms	Urinary Calculus	Demonstrable Bone Involvement	Concomitant Intrinsic Renal Disease	Nephro-Calcinosis	Serum Ca + P mgm/100 cc	Urine Ca.	Adenoma Found at	Length Follow-up	Result
1	W ♀ 41	17 mo.	No	Marked	No	No	13.4 / 1.8	Incr.	Operation	13 yrs.	Well
2	W ♀ 39	3-4 mo.?	No	No	Not proved	No	16.8 / 2.2	Incr.	Operation	11 yrs.	Died Unrelated Cause
3	W ♀ 56	10-12 mo.	No	Severe (Path. Fract.)	No	No	15.4 / 3.8	No test	Operation	6 1/4 yrs.	Well
4	C ♀ 65	Undet.	No	Mild	Severe	Minimal	11.2 / 6.4	No test	Autopsy	----	Died
5	C ♀ 48	11 mo.	Yes	Mild	Severe	Mild	9.4 / 6.6	No test	Autopsy	----	Died
6*	W ♂ 30	12 yrs.	No	Marked	Severe	Severe	10.5 / 11.2	No test	Autopsy	----	Died
7*	C ♂ 23	5 mo.	Yes	Moderate	No	No	13.6 / 3.0	552 mg. / 24 hrs	Operation	1 yr.	Well
8*	C ♂ 7	24 mo.	Yes	Moderate	No	Probably Severe	20.0 / 2.5	Incr.	Operation	18 mo.	Well (Blind)
9*	W ♂ 26	3 yrs.	Yes	Severe (Path. Fract.)	No	None	13.0 / 4.6	Incr.	Operation	3 mo.	Died of Sarcoma
10*	W ♂ 60	Undet.	No	Moderate	Moderate	Moderate	No tests	No test	Autopsy	----	Died
11	C ♀ 37	1 yr.?	No	Moderate	No	No	16.8 / 3.40	Incr.	Operation	3 mo.	Well

* Cases described in detail in text.

a total of eight times between July 15, 1948, and his death 21 months later.

The first blood calcium and phosphorus studies were done on the third admission and were repeated on three subsequent admissions with the following results:

	August, 1948	September, 1949	November, 1949	December, 1949
Calcium (mg./100 cc.)..	10.5	11.1	11.3	9.2
Phosphorus (mg./100 cc.)	7.2	11.2	9.4	16.9
Phosphatase (Bodansky units)	....	16.8	9.6	13.7

Dental films were made Sept. 4, 1948, and only multiple caries were reported. A subsequent review of these films revealed absence of the lamina dura, not recognized during life.

With increasing impairment of renal function, the pain and weakness in the knees and other joints first attributed to rheumatoid arthritis were then related to renal osteodystrophy ("renal rickets"). There were no further episodes of gastrointestinal bleeding, but anemia became steadily more pronounced.

Extreme weakness, muscle atrophy, and, ultimately, mental confusion became prominent. The blood urea nitrogen rose gradually to 165 mg./100 cc. In the final admission the patient had recurrent convulsions. He died March 25, 1950. The clinical diagnoses at death were "chronic renal insufficiency secondary to chronic glomerulonephritis, with renal rickets, pyelonephritis, polyneuritis, muscular atrophy, and arthritis."

At autopsy a 3.0×2.5 cm. adenoma of the right lower parathyroid body was found (Fig. 1*C*). The other three parathyroids were enlarged to dimensions averaging 1.5×0.5 cm., and secondary hyperplasia was present in these to a striking degree (Fig. 1*D*). The kidneys showed severe and advanced nephrocalcinosis (Figure 1*A* and *B*), with marked interstitial fibrosis and parenchymal atrophy. There was no evidence of glomerulonephritis and no reason to doubt that the renal lesion was the direct result of the extensive mineral deposits. The bone showed severe diffuse osteitis fibrosa with demineralization, trabecular resorption, and marrow fibrosis. It may be noted that the shoulder "bursitis" from which he had suffered proved to be a large focus of metastatic calcification ("calcium tophus").

Comment.—This case is an interesting example of a patient under repeated hospital observation more than a period of 12 years, in whom a 3.0×2.5 cm. parathyroid adenoma was not discovered, or even suspected, until autopsy. It illustrates the difficulty of recognizing primary neoplastic parathyroid disease in the presence of long-standing chronic renal disease with sec-

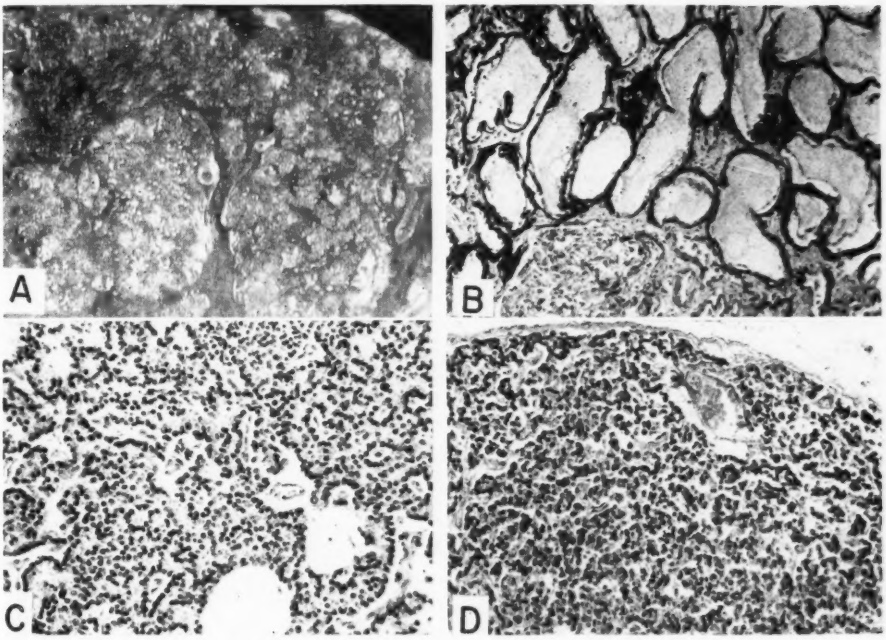


Fig. 1 (Case 6).—*A*, A close-up view of the cut surface of the kidney. Normal markings are obscured. Nephrocalcinosis is highlighted by the innumerable fleck-like calcific deposits which were golden yellow in the fresh state. *B*, Nephrocalcinosis. Photomicrograph of a representative area of kidney stained for calcium deposit (von Kossa stain). Black staining incrustations surround the atrophic tubules. A distorted glomerulus exhibits no stigma of glomerulonephritis. *C*, Parathyroid adenoma composed of chief cells forming both true acini and pseudoacini. A single cystic gland indicates a feature prominent elsewhere in the tumor. *D*, Secondary parathyroid hyperplasia. Section of one of the three enlarged non-neoplastic parathyroids. There is marked numerical increase of chief cells and complete depletion of fat.

ondarily induced parathyroid hyperplasia. This situation may obtain either as a result of primary parenchymal renal pathology or, as in this case, as a result of severe nephrocalcinosis.

The possibility of a biological relationship of hyperplasia as a precursor of neoplasm has long been the subject of speculation and study. Consideration might be given to the possibility that the adenoma found at autopsy in this case, as well as those in Cases 4 and 5 (Table), might have supervened in parathyroid hyperplasia attendant upon chronic renal failure. Albright [1] has commented on the possibility of such a relationship, and Castleman and Mallory [12] have considered it at some length, without definitive conclusions.

In this instance (Case 6) we believe that the histological appearance of the kidneys, the severe nephrocalcinosis, and the advanced bone changes leave little doubt that an actively secreting adenoma initiated the train of events. Moreover, the size and histologic character of the hyperplastic parathyroids were those commonly associated with secondary, rather than primary, hyperplasia.

Since it is generally accepted that a disturbance of the calcium-phosphorus ratio is the common denominator of all phases of parathyroid hyperactivity and since in the phosphorus retention of severe renal disease, leading to secondary hyperparathyroidism, the serum calcium usually falls, one other point seems to support the conclusion that in this case the functioning adenoma preceded the renal disease. It is noted that this patient's serum calcium did not fall to a "normal" level until very late in the course of the disease (three months before death)

and then only to 9.2 mg/100 cc. The concurrent serum phosphorus level was 16.9 mg/100 cc. Downs and Scott [16] have recorded a similar case which was referred to by Albright and Reifenstein as the only case of its kind that had come to their attention. It seems possible that failure of the serum calcium to reach a lower point may represent a means of distinguishing secondary hyperplasia complicating banal renal disease from that occurring in nephrocalcinosis due to functioning parathyroid adenoma. In the former instance calcium values in the tetany range are common. This may not be the case when the powerful impetus of an active adenoma continues to bring large amounts of calcium from the osseous depots.

Finally, it may be noted that this patient had a recalcitrant peptic ulcer, as did two other patients in the series (Cases 4 and 11). Haynes,* on the basis of studies prompted by the previous reports of Rogers and his associates,[27] found that 24% of the Mayo Clinic patients with proved hyperparathyroidism had associated peptic ulcer at some time in the course of their disease. The relationship, direct or indirect, of peptic ulcer and parathyroid disease is, of course, tenuous, but Black [10] points out that patients in whom both conditions are present are refractory to ulcer treatment until after the parathyroid disease has been corrected.

Case 8.—A seven-year-old Negro boy was said to have been sickly "all his life." The details of his history are not entirely clear. He had been hospitalized in another state about a year prior to this admission, because of listlessness, apathy, and malnutrition. The initial local admission was on Nov. 11, 1953, when the patient was so weak and his knees so stiff that he could not rise from the floor. He was feeble and emaciated and displayed marked nuchal rigidity. An elevated spinal fluid protein and cell count together with a positive serologic test for syphilis led to a diagnosis of central nervous system syphilis. Joint manifestations were attributed to rheumatoid arthritis. He suffered repeated episodes of vomiting and had a number of generalized convulsions.

After antisyphilitic therapy he was sent to a convalescent home but remained hopelessly weak and continued to have repeated attacks of vomiting and convulsions. He was readmitted to the hospital on Dec. 24, 1953, and at this time serum calcium and phosphorus studies showed levels of 20 mg./100 cc. (10 mEq.) and 2.5 mg/100 cc. (1.47 mEq.) respectively. Serum alkaline phosphatase was 23 Bodansky units. It was noted on this admission that the child had become blind, but repeated examinations by ophthalmologists and neurologists failed to elicit the cause of the amblyopia. There was no papilledema and only very questionable optic atrophy. Radiological studies showed absence of the lamina dura, diffuse skeletal demineralization with osteitis fibrosa cystica, and a left renal calculus. The latter had not been present in films taken on the first admission.

Although the child's condition was extremely precarious, operation was undertaken, with elaborate supportive precautions, and a 2.5×1.0 cm. clear-cell adenoma (Fig. 2.1) was found and removed from behind the middle third of the right lobe of the thyroid. Because of the patient's poor condition a tracheotomy was done.

Although postoperative convalescence was slow, it was surprisingly smooth. By the 10th postoperative day the serum calcium and phosphorus levels were 7.6 and 1.6 mg/100 cc.† and the alkaline phosphatase was 3.91 Bodansky units. The mineral values rose to a plateau in the next few weeks, with the serum calcium maintained at 11.6 mg/100 cc. and the serum phosphorus at 6.6 mg/100 cc. There was strong evidence of renal damage and a pronounced hypertension, present before operation, which persisted afterward in the range of 160/100 to 180/130.

The child's nutritional state and general health, both mental and physical, improved strikingly, but there has been no improvement in his vision.

Comment.—This case is believed to represent one of the youngest patients on record with proved parathyroid adenoma. It is ironical that the correct diagnosis was missed until more than two months after he came under hospital observation, in part because his youth militated against consideration of hyperparathyroidism. In addition, a change in laboratory routine resulted in reports of serum calcium and phosphorus levels in milliequivalents instead of the method of indicating milligrams per 100 cc., and the

* Cited by Black.[10]

† It is commonly observed in patients with hyperparathyroidism with bone disease that the serum phosphorus falls temporarily after operation, while in those without bone disease it rises promptly. The explanation for this is not clear, but it is assumed that the phosphorus is being held somewhere in the regenerating bone.[1]

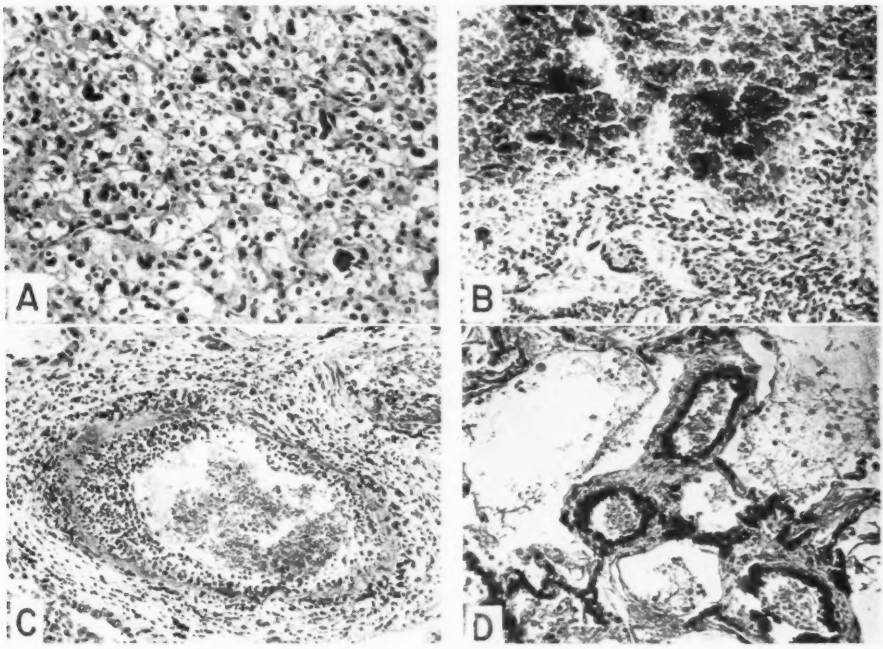


Fig. 2.—*A*, (Case 8) In this adenoma the cells are largely of the water-clear (wasserhelle) variety. They exhibit much pleomorphism, a quality which is shared by the nuclei. The latter are hyperchromatic, and occasional mitotic figures are encountered. *B*, (Case 10) Necrosis and calcification in the parathyroid adenoma. The epithelial residua may be seen below in process of necrosis. The upper portion of the photomicrograph reveals coarse calcium deposits with inflammatory exudate. Hematoxylin and eosin stain, × 160. *C*, Necrotizing angiitis of a medium size pulmonary artery. An acute inflammatory exudate extends throughout the wall and adventitia. The smudgy material in the media represents a zone of necrosis related to fine calcific spicules. Hematoxylin and eosin stain; × 160. *D*, Silver impregnation highlights the calcium deposits in pulmonary alveolar and blood vessel walls. This is accompanied by severe edema and an exudate of fibrin and neutrophiles. Von Kossa stain; × 160.

values were mistakenly interpreted as normal (Ca, 10.0 mEq; P, 1.47 mEq.). The error was finally recognized by an alert house officer, and the diagnosis was thus established. Meanwhile the child had become blind. Although the explanation for the visual defect has defied precise interpretation, there has been speculation that this might be due to calcium deposits in the visual centers of the posterior cerebrum. Calcific deposits in the lungs, stomach, cornea, thyroid gland, and other soft tissues (in addition to the familiar nephrocalcinosis) have been observed in association with hyperparathyroidism (Case 10), but we have found no instance of proved cerebral calcification. Radiopaque deposits were not demonstrable in roentgenograms of the skull but might have been obscured by overlying bone. The patient has improved in other respects since operation, but the blindness and the impaired renal function have persisted unchanged. Anspach and Clifton[2] reported blindness associated with primary hyperparathyroidism in an 11-month-old infant but offered no explanation for it. The relationship between severe parathyroid hyperfunction and blindness in both their case and ours seems much more than coincidental. If, as we have assumed, it is due to calcific deposits in the cerebral visual centers, the possibility of recovery or even improvement, after otherwise effective treatment, would seem (as it is for nephrocalcinosis) to be very remote.

CASE 9.—A white man, aged 26, was admitted to the hospital Aug. 18, 1950, wearing a cast on his left leg.

Though a good athlete in high school and subsequently employed as a sheet-metal worker, the patient had been declared 4-F by his Draft Board because of a left-sided limp which had been present since childhood. About three years prior to admission he noted slowly increasing weakness, polydypsia, and polyuria. A year later he sustained a fracture of the left humerus from a trivial fall. This had healed spontaneously. Four months later he had another minor fall at home and suffered fractures of the left tibia and fibula and a new fracture of the left humerus. In another hospital these were recognized as pathological fractures, and after appropriate studies a diagnosis of "parathyroid disease" was made. According to the patient, he was advised that "no one would dare operate on him" and an undetermined amount (250 r) of x-ray therapy was administered over the neck. Casts were applied to the fractured extremities. Maggots appeared in the leg cast, thus precipitating hospital entry, and examination revealed soft tissue ulceration over a large tumor at the fracture site.

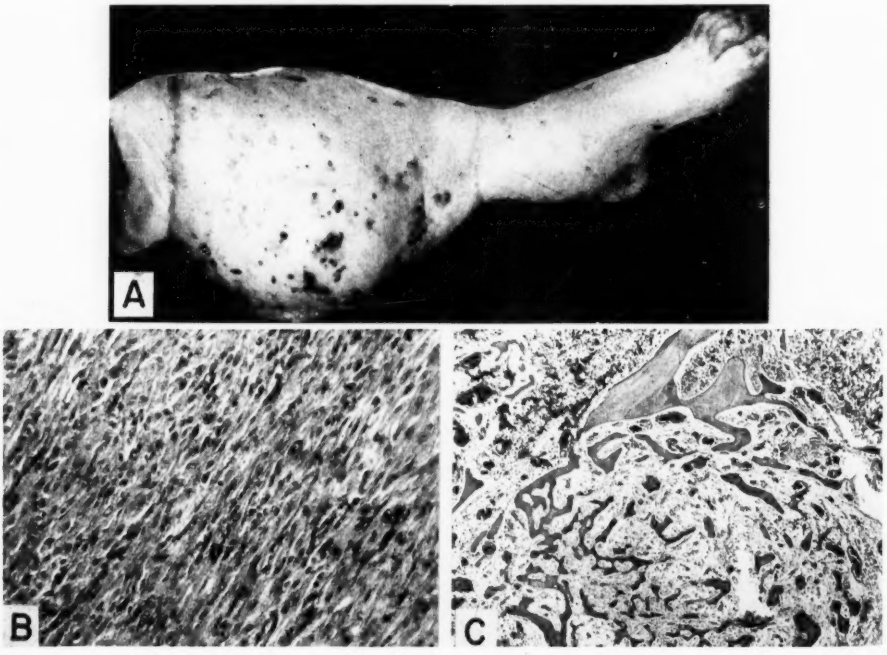
At this admission the serum calcium levels ranged from 9.6 to 10.5 mg/100 cc. and the phosphorus from 2.5 to 1.3 mg/100 cc. On one occasion the serum alkaline phosphatase level was 22.3 Bodansky units.

Fibrocystic changes and patchy demineralization were demonstrated by roentgenography in the clavicles, humeri, skull, femora, and left tibia. Multiple pathological fractures were present, and the lamina dura was absent in dental films. There were cystic changes suggestive of "giant-cell tumor" in the left humerus and left tibia, the masses measuring 7.5 and 4.5 cm. respectively. Multiple renal calculi were demonstrated.

Cervical exploration was performed on Sept. 1, 1950, and a parathyroid adenoma, weighing 5 gm. and measuring 2.5×2.0×1.5 cm., was removed from behind the left lower pole of the thyroid gland.

Convalescence from this operation was uneventful, and by the 25th postoperative day the serum calcium was 7.8 mg/100 cc. and the phosphorus 2.2 mg/100 cc. The ulcerated lesion over the left tibia (in which the maggot infestation had been abated) failed to improve and became increasingly painful. A biopsy showed a "malignant giant-cell tumor," and on Sept. 27, 1950, twenty-six days after parathyroidectomy, a supracondylar amputa-

Fig. 3 (Case 9).—*A*, Amputation specimen, left leg. Marked swelling and deformity are due to fibrosarcoma of the tibia. *B*, Spindle-cell Fibrosarcoma. Photomicrograph of amputated tumor of tibia. Neoplastic nuclei are varied in size and configuration. Mitotic figures are abundant. *C*, A section of bone marrow procured at autopsy two and one-half months after removal of parathyroid adenoma. Osteitis fibrosa remains manifest but there is evidence of reossification within the fibrous stroma. Though not evident at this magnification, each newly formed bone spicule is surrounded by a layer of osteoid.



tion was done (Fig. 3*A*). Further study of the specimen confirmed the diagnosis of sarcoma arising in the left tibia. The lesion proved to be a fibrosarcoma (Fig. 3*B*), although in several areas there were large numbers of giant cells identical with those seen in the giant-cell tumor of bone. The patient's condition deteriorated steadily, and by Nov. 10, chest films, previously interpreted as negative, revealed multiple metastases. He died on Nov. 16, 1950, three months after admission.

At autopsy, no additional parathyroid tumors were found. Extensive metastatic sarcoma was present in both lungs, the mediastinal nodes, and the liver. A total of 10 renal calculi was present in both kidneys, which were the seat of pyelonephritis but showed no parenchymal calcinosis. Widespread cystic degeneration accompanied the healing osteitis fibrosa in the vertebrae, ilium, and remaining long bones (Fig. 3*C*). The head was not examined.

Comment.—As far as we can ascertain, this case is unique with respect to the development of malignant neoplasm in a bone presumably the seat of osteitis fibrosa cystica of parathyroid origin. A reasonably thorough search of the literature has failed to reveal a similar case. Some of the pioneer reports refer to "giant-cell sarcomas," but we have failed to find an authentic example of malignant neoplasm. Barr, Bulger, and Dixon [5] (1929) refer to "multiple cystic bone tumors, several of which on pathologic examination have been found to be giant-cell sarcomas." We believe this designation and others like it to be due to histologic interpretations current at that time but unacceptable now. Gordon-Taylor [19] performed a hip disarticulation in 1929 on a 20-year-old woman with a diagnosis of femoral sarcoma. He recognized the error and himself removed a parathyroid adenoma six months later. Beck ‡ is reported to have performed two amputations (1928) under similar circumstances. Mandl [22] mentions sarcoma (necessitating amputation) developing in an area of "osteitis fibrosa localisata" in the sister of a young man with proved parathyroid adenoma. Since there is a recognized § familial incidence of primary hyperparathyroidism, this patient might be comparable to the one here reported, but the evidence is indirect.

The "brown tumors" which, prior to the recognition of the relationship of the various bony changes to hyperparathyroidism, were regularly classified as "giant-cell tumors" are now correctly attributed to the effect of excessive parathyroid hormone on bone structure. They are considered to be simply local exaggerations of the diffuse skeletal disease. Hunter and Turnbull (1931) termed them "osteoclastomas," but Albright and Reifenstein consider the expression "osteoblastoma" preferable.[1] A malignant tumor stemming from such a lesion might relate to the active bone-forming elements (osteogenic sarcoma) or the fibrous components (fibrosarcoma). Osteoclasts are not currently considered to be the basis for true giant-cell tumors of bone, and there is no malignant neoplasm known to be derived from them. The tumor in the present instance proved to be an anaplastic fibrosarcoma with no evidence of osteogenic activity.

A direct causal relationship between osteitis fibrosa and fibrosarcoma is, of course, speculative. The sequence of long-standing hyperparathyroidism (at least three years), diffuse bone disease with pathological fractures, and sarcoma apparently arising at the site of one of these fractures lends some weight to the presumption of relationship. The fact of trauma in such a circumstance may represent the motivating stimulus. Acute trauma as a cause or precipitating factor in bone and soft-part sarcoma has been actively debated in the literature. Whether the preexisting bone disorder, the injury by itself or in conjunction with metabolic skeletal disorder, or simply a coincidental and independent neoplasm arising *de novo* represents the explanation is a matter for conjecture. The occurrence of osteogenic sarcoma as a sequela of Paget's disease is a well-documented phenomenon. There is much parallel in the degree of osteoblastic and fibroblastic activity in Paget's disease and in von Recklinghausen's disease of bone. One might wonder, however, if this parallel has signifi-

‡ Beck,[7] cited by Ballin.[8]

§ References 17 and 18.

cance, why neoplastic complications of bone have not been more commonly encountered in hyperparathyroidism.

CASE 10.—A 60-year-old white bartender, admitted Feb. 1, 1955, in a semicomatose state. A fragmentary history assembled from various sources indicated that the patient was a chronic alcoholic who had been suspected of having long-standing liver disease. It was reported, with doubtful reliability that he had been "apparently well" until two to four days before he was brought to the hospital, during which period he had suffered with malaise, vomiting, and inability to eat.

His admission temperature was 100 F, his pulse rate was 118, and his respiratory rate was 24. His blood pressure was 120/70 mm. Hg. Physical examination showed a normally developed, moderately obese man of about 60 who responded to questions only with moaning and unintelligible mumbling. There was no evidence of trauma or existing alcoholism. Aside from these general observations, physical examination revealed only moderate abdominal distention and a fecal impaction. Neurological examination demonstrated generalized muscular weakness, but there were no localizing signs.

Special studies, including the usual blood-cell counts and stained smears, two batteries of liver-function tests, serum-electrolyte determinations, a lumbar puncture, and serological tests for syphilis, were all within the normal range. Urinalyses showed specific gravities ranging from 1.010 to 1.012, and the blood urea nitrogen rose from an initial 59 mg/100 cc. to 124 mg/100 cc. in seven days. Albuminuria was consistently present (4+), as were occasional granular casts. One examination of the stool for occult blood was negative.

Roentgenological examination included plain films of the chest and abdomen on two occasions, and these were uninformative.

The patient did not respond to various supportive measures. On the fourth hospital day his temperature rose to 105.2 F and displayed an irregular spiking curve thereafter, with a proportionately increased pulse rate. Blood and urine cultures were negative. The patient died quietly on the seventh hospital day, without regaining consciousness, and the final clinical diagnosis was "probable hepatic coma."

On the day of his death serum sodium, potassium, calcium, and phosphorus determinations were requested. The first two values were Na, 137 mEq/Liter and K, 3.9 mEq/Liter, but the blood sample was, unfortunately, inadequate and the calcium and phosphorus determinations were not done; hence, no clinical data with respect to parathyroid function are available.

At autopsy a large (5×3×2 cm.) cystic and hemorrhagic parathyroid adenoma was found in contiguity with the right lower pole of the thyroid. The lungs were heavy and were the seat of what appeared to be coalescent pneumonic consolidation. The heart was enlarged and beefy and weighed 480 gm. Peculiar tan flat plaques were noted in the endocardium, and whitish gritty flecks were encountered in the myocardium. The liver weighed 3060 gm.; it displayed a uniform finely nodular cirrhosis. The spleen was enlarged, weighing 480 gm., and contained a large polar infarct. The kidneys together weighed 430 gm. They were symmetrical and grossly unremarkable. Soft-tissue deposits were not observed and there were no calculi.

On microscopic examination the parathyroid adenoma (Fig. 2*B*) proved to be of chief-cell solid alveolar pattern. The hemorrhage noted in the gross was related to foci of necrosis in which large, amorphous calcareous masses were deposited. Similar calcific foci were present in the thyroid.

In the lungs there were fine spicular deposits in alveolar septa and small blood-vessel walls. In the latter instance a necrotizing angiitis resulted (Fig. 2*C*). The alveoli contained abundant edema fluid, much fibrin, and a spotty exudate of neutrophiles. Von Kossa stains clearly demonstrated that the crystalline material was calcium (Fig. 2*D*). There were similar foci of calcinosis in the myocardial interstices, in the region of the subendocardial plaques, and in the basement epithelium of renal tubules. Related in each of these areas was an inflammatory infiltrate of varying intensity.

Sections of bone marrow exhibited generalized osteitis fibrosa of moderate severity, with trabecular resorption and thin fibrous seam replacement. A spotty, but severe, necrotizing inflammation appeared in the myocardium, pancreas, and kidney. It was believed that these were probably related to inapparent mineral deposits. There was also a frank active portal cirrhosis, obviously unrelated to the parathyroid disease.

Comment.—The autopsy findings in this case are characteristic of the syndrome known as parathyroid poisoning. Albright and Reifenstein have summarized the subject well. They refer to the classical experimental studies of Collip (1926), in which typical calcific deposits in the stomach, thyroid, lungs, and kidneys were produced in dogs by administration of massive doses of parathyroid hormone. Collip's observations have been confirmed and extended more recently by Cantarow, Stewart, and Howsel,[11] in dogs and by Oliver,[25] in rats. The manifestations in our patient almost exactly parallel those recorded in Dawson and

Struther's case, which is cited by Albright, and are very similar to those in the second of Oliver's two cases. According to Young and Emerson,[30] only 10 cases had been recorded up to 1949, with but 1 patient surviving. Their patient had parathyroid carcinoma.

Thus, although parathyroid poisoning is unusual, the reported cases have been thoroughly studied. Its clinical and pathological characteristics are well recognized and can be induced in experimental animals. The present discussion, therefore, need not be prolonged by a detailed review.

It is pertinent, however, to note that the critical serum calcium level ranges between 17 mg/100 cc.[1] and 20 mg/100 cc.,‖ but extreme hypercalcemia alone does not, apparently, suffice to produce the "chemical death" of parathyroid intoxication. The other essential seems to be sufficient renal impairment to produce a sharp concurrent rise in the serum phosphorus level. In Case 6, of this report, the phosphorus level was high enough, but the calcium was not, while in Case 8 the reverse was true, raising some doubt as to the validity of the cerebral calcium deposits, postulated as the cause of the patient's blindness. It is unfortunate in the present instance (Case 10) that serum calcium and phosphorus determinations were not requested until too late. The "poisoning" phase of this patient's disease was evidently fairly acute, in view of the fresh degenerative changes, the hemorrhage necrosis, and the rather intense polymorphonuclear infiltration in the affected tissues.

Nevertheless, it is debatable whether or not prompt recognition could have saved the patient's life. Since his feedings during the seven days he survived were parenteral and calcium-free and since the blood urea nitrogen rose steadily in spite of this, it may be argued that his disease was irreversible on admission. Such retrospective analysis is useful chiefly because it serves to reinforce our already strong conviction that serum calcium and phosphorus determinations should be employed with much greater frequency than is usual in most clinics. This is especially true in the presence of a diagnostic problem that is made more difficult by an unavoidably inadequate history and uninformative physical findings. In such circumstances an array of "range-finding" laboratory tests is usually requested promptly, but all too frequently serum calcium and phosphorus determinations are not included. A Sulkowitch test might have provided the necessary clue in this case, but, since numerous blood samples were being drawn for other studies, the inclusion of serum calcium and phosphorus levels would have established the diagnosis at once.

GENERAL COMMENT

Aside from the four unusual cases, which have received individual comment, experience with so small a series does not justify generalizations or conclusions not already widely recognized. In particular, we can add nothing to the numerous excellent accounts of operative techniques, by various authorities.¶ In only one instance was the adenoma found in an unusual location. In Case 11 the parathyroid adenoma was removed from between the trachea and the esophagus, on the right side.

However, the material here reviewed has seemed to us to merit at least one inferential deduction in this connection. We are in hearty accord with the emphasis that has been placed on the potential, and often actual, technical difficulty of successful therapeutic parathyroidectomy. It is possible, nevertheless, that the well-founded warnings of so many authors may have had some unsought and untoward consequences. The formidableness of parathyroid surgery has apparently so impressed both physicians and laymen that some patients may be deterred from seeking proper treatment. Case 9 is an example of this situation, where the patient was actually advised not to have an operation which might have saved his life if it had been done in time. It is plainly im-

‖ Haynes, A. L., cited by Black [10]; Reference 28.

¶ References 8, 9, 13, 14, 21, and 26.

practical, for economic and other reasons, to refer all patients in whom a diagnosis of primary hyperparathyroidism has been made to centers where a large experience in this field has been acquired. Parathyroid surgery is a skill which should be within reach of all who need it, and it can be developed in any hospital or medical center where the over-all surgical standards are high. The surgeon who undertakes it must have adequate general training and experience, and he should conscientiously prepare himself by careful study and, if possible, by cadaver dissection, before attacking his first parathyroid adenoma; but he should not deny a patient his chance of cure because the patient is unable to go to a distant center. The development, in any given community, of keener diagnostic acumen with respect to parathyroid disease would fall short of its purpose and value if adequate treatment is not made available to patients in whom the disease is found.

Finally, with reference to the plea made in 1945 by McClure and Lam [23] for more reports of long-term results, it may be noted that three of the patients in this series remained free of parathyroid disease for 6 (Case 3), 11 (Case 2), and 13 (Case 1) years, respectively, and that none of them had shown evidence of renal damage at the time of operation. Cases 7, 8, and 11 are too recent to be called "long-term," though the ultimate outlook in Case 8 is almost certainly unfavorable. The patient in Case 6 was observed over an elapsed period of 12 years. His was the end-result which may be considered characteristic of those instances in which the diagnosis is not made until renal damage is irreversible.

These cases collectively serve to emphasize again the obvious conclusion that the diagnosis must be made and operation performed before serious renal damage has occurred if a favorable long-term result is to be achieved.

SUMMARY

Out of a series of 11 cases of parathyroid adenoma, 4 cases are sufficiently unusual to merit individual review and comment. One of these occurred in a seven-year-old boy in whom blindness is a concurrent and apparently related complication. Another case was complicated by the development of a fatal fibrosarcoma in what is believed to have been originally an area of osteitis fibrosa cystica of hyperparathyroidism. In a third case, true neoplastic parathyroid adenoma occurred in association with secondary parathyroid hyperplasia, the latter the result of nephrocalcinosis. The fourth case was one of parathyroid poisoning—the so-called "hyperhyperparathyroidism" of Albright. The remaining cases followed conventional patterns.

No sweeping conclusions can be derived from this limited group of cases, but certain deductions have been drawn which are believed to merit consideration and publication.

The authors wish to record their thanks for cooperation and assistance to the Directors of the Laboratories of Pathology of the Jewish Hospital, Cincinnati (Cases 1 and 2); the Edwin F. Brown (VA) Hospital, Dayton, Ohio (Case 7), and St. Elizabeth Hospital, Covington, Ky. (Case 9).

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DISCUSSION

On Papers by Dr. Melvin A. Block and Brock E. Brush; C. Marshall Lee, Jr., Edward A. Gall, and W. Thomas McElhinney

Dr. B. Marden Black, Rochester, Minn.: It is most gratifying to see more interest being taken in hyperparathyroidism. The condition is still being largely overlooked, particularly by urologists, in spite of the fact that fully 5% of all cases of renal lithiasis and possibly 15% to 20% of cases of recurrent lithiasis result from it. While the cases reported by Dr. Lee are most interesting, they are also most unusual. It could well be reemphasized that in the usual case of hyperparathyroidism the only symptoms are those associated with stones in the urinary tract.

[Slide] Among the first 112 cases in the Mayo Clinic series, urinary complications had developed in 83%. Among current cases, osseous complications are present in probably not more than 1 case in 20.

Successful screening of patients with urinary lithiasis for hyperparathyroidism is admittedly difficult. It may well be that some such test as those described by Drs. Block and Brush today will prove superior to simple determinations of calcium and phosphorus in the serum. However, in the experience of the Clinic to date, careful determinations of serum calcium and phosphorus have proved more discriminatory than the far more complex tests currently being evaluated.

[Slide] A precautionary word might be added regarding surgical treatment. This slide is a reproduction of plates accompanying Sandstrom's original description of the parathyroid glands. Their position and size are shown beautifully. As Churchill stressed some 20 years ago, some experience in the recognition of parathyroid glands should be gained before attempting to operate for hyperparathyroidism. The immediate aim of the surgeon should be the finding of four parathyroid glands, since in no other way can one be certain that multiple adenomas or wasserhelle hyperplasia is not being overlooked.

Bridging Defects in Large Arteries

A Problem for Arteriogenesis

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and
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The search for a simple and ever-ready material for bridging defects in large arteries, to reestablish the flow of arterial blood to the distal parts of an extremity or to vital structures of the body, has been pursued by investigators for many decades. In 1900 Payr [1] published the results of experimental studies with absorbable and nonabsorbable materials and he concluded that collars and tubes of absorbable magnesium, lined by autogenous venous grafts, functioned satisfactorily when used to bridge defects in large arteries. In 1906 Carrel [2] studied the problem of suturing blood vessels and later used autogenous venous grafts, homologous arterial grafts, and heterologous arterial grafts to bridge defects in arteries in animals. The first World War gave Tuffier [3] an opportunity to use tubes of various metals to bridge defects of large arteries produced by wounds of war.

In the decade 1930-1939, our [4] attention was centered around the problem of stimulating collateral arterial circulation in patients with structural changes in peripheral arteries. During this period, many longstanding arteriovenous aneurysms were treated satisfactorily by quadruple ligation and excision of the arteriovenous fistula,[5] whereas longstanding arterial aneurysms were treated successfully by introducing fine wire into the aneurysmal sac, surgically obliterating the aneurysmal sac, or extirpating the entire aneurysm without reestablishing the continuity of the major artery. During World War II, however, the wounds of violence which occurred from high velocity bullets or fragmentation bombs frequently involved great blood vessels and in a large series of wounded soldiers with extensive damage of the popliteal artery loss of the extremity resulted in about 75% of the cases. It became apparent from the war reports of DeBakey and Simeone [6] that the continuity of major arteries should be restored as soon as possible after extensive damage caused by any wound of violence. The reports of Jahnke and Seeley,[7] during the Korean campaign, indicate that reestablishment of continuity of the popliteal artery at the battlefront by use of autogenous venous grafts reduced the incidence of the complication of gangrene of the extremity to about 10%.

Bridging defects in larger arteries, especially the arteries where greater intraluminal pressure exists, presented other hazards. To provide this additional strength in a graft, surgeons naturally turned to the use of fresh or preserved segments of large arteries from other human beings, even though homologous grafts of all other living tissues have failed to retain their original function when transplanted into man. The technical, biologic, and legal problems incident to obtaining, sterilizing, storing, and implanting such homologous arterial grafts presented further obstacles to their universal use. Volumes of scientific reports have accumulated on this aspect of the subject alone.

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It was only natural for investigators to turn again to the fundamental aspects of the problem and search for more suitable and more easily obtainable substances. Again the products of modern metallurgy, body tissues, animal secretions, and organic chemical compounds were fashioned into tubes and used to replace large arteries in animals, with varying degrees of success.

Soon thereafter the chemists began to make available, for experimental use, several varieties of plastic sheets and fibers which rival silk and metals in strength, smoothness, and inertness. Body tissues tolerated these plastic substances even better than fibers of animal origin. Just as our surgeons of a generation ago used silver tubes, magnesium tubes, and even glass tubes, so now surgeons began to use tubes of impervious plastic materials, with or without a lining of autogenous tissue, to bridge defects in large arteries. These, too, proved reasonably successful, and, because of their smooth lining and their blood-repellent properties, they functioned as replacements for segments of large arteries of the neck or extremities, with relatively few complications. Hufnagel,[9] Shumacker,[10] and their associates have been interested in the use of impervious plastic materials, and their studies have added much to our knowledge of the biologic reaction to these synthetic substances.

Our past experience in the field of vascular surgery has convinced us that this problem is a physiologic rather than an anatomic one. Physiologically speaking, defects in large arteries must be bridged by autogenous tissues or by an elastic frame of some inert and pervious material through and about which the body cells can proliferate and form permanent protective layers.

Voorhees, Jaretzki, and Blakemore[8] offered a truly physiologic approach to this problem when they demonstrated that closely woven cloth of some of the synthetic fibers permitted the autogenesis of arterial coats of fibrous tissue, with the plastic cloth tube serving as the elastic layer of the new artery. This, we believe, is a fundamental contribution to the problem of arterial replacement, and our experience in the laboratory with fine meshes of various synthetic fibers has convinced us that "arteriogenesis" by this means is not only possible but may be a practical solution for some of our most perplexing vascular problems.

We believe that the remarkable ability of the plastic cloth to bring about "arteriogenesis" depends upon the physical property of being pervious as well as elastic. We have used cloth woven from various synthetic fibers; namely, nylon, Dacron, Orlon, and Vinyon-N. However, during the past 10 months, Doctor Bollack and I have used only

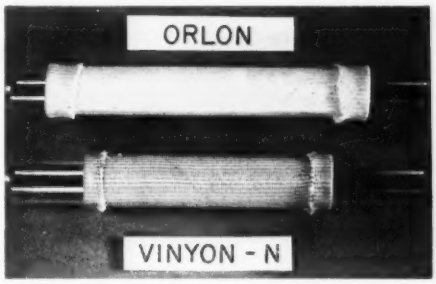


Fig. 1.—Woven tubes of synthetic materials, showing the turned-back cuff, which makes the anastomosis with an artery much simpler.

cloth or woven tubes of Orlon and Vinyon-N (Fig. 1), and our experiments with these two materials form the basis for this report.

EXPERIMENTAL STUDIES

We used 17 young dogs weighing between 35 and 40 lb. each. In seven of these dogs, we simply sewed a patch of Vinyon-N cloth over the defect in the aorta. In five of the dogs, segments of abdominal aorta were replaced by tubes woven of Vinyon-N fiber, and, in five other dogs, similar tubes of Vinyon-N and Orlon were used to bridge defects in the thoracic aorta.

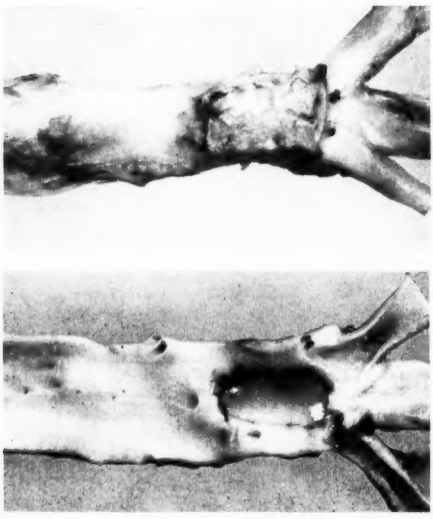
Patch Grafts.—In the seven animals in which patch grafts were used (Table 1), we employed the following method. The abdominal aorta was freed so that Potts-Smith aorta clamps could be applied above and

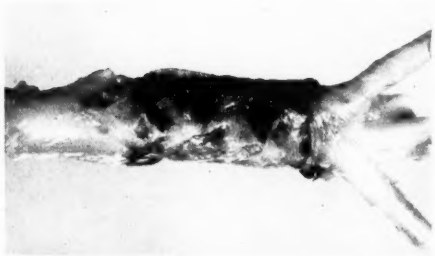
TABLE 1.—*Patch Grafts on Aorta*

Dog No.	Course
201	Killed after 135th day; paraplegia persisted for 10 days after operation
220	Operated on Oct. 6, 1954; good femoral pulses
226	Killed after 40th day
235	Killed after 30th day
241	Killed after 97th day
262	Killed after 80th day
265	Operated on Oct. 27th, 1954; good femoral pulses

below the site for the graft. The anterior surface of the aorta for distances of 1 to 2 in. was resected, and the defect in the aorta was covered with a patch of Vinyon-N cloth and sewed in place by mattress sutures or continuous sutures of 00000 nonabsorbable (silk) sutures on Atraumatic needles. In one of the animals (No. 201) the patch was too small, and so, when the fixation by sutures was finished, the lumen of the aorta was greatly narrowed and temporary weakness of the hind legs resulted. This weakness of the muscles lasted about 10 days, then slowly disappeared. The animal lived without further complications and was killed after 135 days. Coarctation of the aorta existed at the level of the graft, but there was no evidence of thrombosis at the site of the patch graft or in any of the major arteries of the extremities. Four of the remaining animals were killed between 40 and 97 days after operation. All the patch grafts were successful, and there was no evidence of clotting of blood on or near the grafts. The lining was smooth and glistening, and the outer coat of the artery was made up of dense fibrous tissue (Fig. 2). No aneurysmal dilatation at the site of the patch grafts was found in any of the animals. Two animals of this series are living and well at this time. Both have good femoral pulses.

Fig. 2.—Photograph of the terminal aorta, showing the repair of a defect with Vinyon-N cloth. Animal killed 97 days after operation. No evidence of thrombosis or weakness of the new wall.





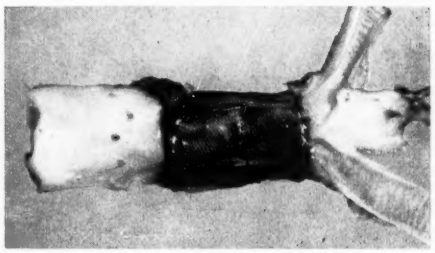


Fig. 3.—Photograph showing the bridging of a defect in the terminal aorta. Animal killed 73 days after implantation of the synthetic tube. No evidence of thrombosis.

Abdominal Aortic Grafts.—In this series of five dogs (Table 2), we freed the abdominal aorta from the trifurcation to the renal arteries and then excised segments of the

TABLE 2.—*Grafts into Abdominal Aorta*

Dog No.	Course
292	Killed after 90th day
320	Killed after 73d day
389	Killed after 40th day
391	Killed after 70th day
392	Operated on Nov. 24, 1954; good femoral pulses

TABLE 3.—*Grafts into Thoracic Aorta*

Dog No.	Course
420	Died on 6th postoperative day; autopsy: no thrombosis in the aorta, bilateral pneumonia
455	Operated on Dec. 13, 1954; good femoral pulses
464	Operated on Dec. 20, 1954; good femoral pulses
490	Killed after 30th day
571	Operated on Feb. 9, 1955; good femoral pulses

aorta varying in length from 1½ to 3 in. Tubes woven of Vinyon-N fiber were used to bridge these defects in the aorta. The turned-back cuff of the tube made implantation by end-to-end suturing with 00000 silk easier. All animals survived without complications. Four animals were killed at intervals varying from 40 to 90 days for special study of the process of arteriogenesis (Fig. 3). One animal (No. 392) is still living and well and has good pulses in both femoral arteries.

Fig. 4.—Photograph showing the tube of Vinyon-N used to replace a long segment of thoracic aorta in a dog. No evidence of bleeding through the meshes of the tube.

Thoracic Aortic Grafts.—All five animals of this series (Table 3) were operated upon with use of hypothermia produced by ice-water baths. The animals were all anesthetized with pentobarbital (Nembutal) intravenously, and the degree of cooling of the body was measured by a thermocouple in the esophagus of the animal. The temperature was kept between 75 and 83 F during the time the thoracic aorta was completely occluded, which ranged from 40 to 60 minutes. After the tube of Vinyon-N or Orlon had been sutured in place to bridge the defect in the aorta, the Potts-Smith aorta clamps were removed—first the distal one and then the proximal one. A few pearls of blood exuded through the wall of the plastic tube, but, with gentle pressure with a gauze sponge, all bleeding ceased within 20 to 30 seconds (Fig. 4). The first dog of this series died on the sixth postoperative day, and autopsy showed bilateral pneumonia. The graft functioned normally, and there was no evidence of thrombosis either within the graft or in any of the neighboring arteries. All the rest of the animals in this series were given antibiotic substances for five to seven days after operation, and no further complications arose. One animal was killed on the 30th postoperative day. The woven plastic tube was completely encased in firm fibrous tissue, and the lining was a thin layer of glistening material which grossly could not be distinguished from the intima of the remaining parts of the aorta. Three animals of this series are still living and well, and all have good femoral pulses which can be palpated without difficulty. We have not had to remove fluid from the chest in any of these animals.

HISTOLOGIC STUDIES

Sections of the aorta at the junction with these plastic tubes have shown that the Orlon or Vinyon-N is very quickly covered by a firm layer of fibrous tissue which is an extension of the outer coats of the aorta. The inside lining of the plastic tube is made up of a thin layer of cells which appear to be fibroblasts. These fibroblasts are seen to extend from the outer layers through the meshes of the plastic cloth. Within six days a well-formed layer of these fibroblasts lines the plastic tubes, and this layer is continuous with the intimal lining of the aorta above and below the graft. The blood-repellent properties of these plastic fibers could be responsible for the fact that thrombosis does not take place immediately, as it does in tubes of metal and animal products.

There is no cellular reaction around the fibers of Orlon or Vinyon-N, while there are

occasional giant cells about the silk sutures which are used to hold the graft in place. We are now interested in using Orlon or Vinyon-N fibers to fix the graft in place.

COMMENT

In experiments on dogs we have used Orlon and Vinyon-N in the form of patches of cloth and tubes made of the cloth or woven tubes of greater thickness and strength (Fig. 1). The bleeding through the meshes of the cloth of Vinyon-N, which has been mentioned by Voorhees, Shumacker, and Hufnagel, is related to the kind of weave, as well as to the physical character of the fiber itself. Orlon fiber is smoother and finer and can be woven tighter; consequently, it does not permit "bleeding through the mesh" and has therefore been preferred by many investigators. Both Orlon and Vinyon-N cloth are well tolerated by the body tissues, and both possess a degree of elasticity which closely approximates that of the elastic layer of the aorta. Numerous attempts have been made to fashion tubes with branches or a facsimile of the aortic bifurcation. The hand-fabricated tubes make functional segments, but several investigators (Voorhees, Blakemore, Hufnagel, and ourselves) believe that seamless tubes of these fibers, in various sizes, shapes, and with desired branches for renal arteries, common iliac arteries, and even smaller arteries, will be fabricated by some ingenious person within the near future.

The histologic studies indicate that the pervious and elastic matrix has served as a framework upon which body cells, principally fibroblasts from the periarterial or retroperitoneal or retropleural tissues, have been able to proliferate through the meshes. This gives a smooth layer of fibroblasts, which serves as the intima, with heavy coats of fibrous tissue outside the plastic mesh to serve as protective coats of the new artery. We believe this is arteriogenesis and should be an ideal method for replacing even long segments of the aorta, since the functional layers appear to be developed from without inwardly. The new intima is not produced by ingrowth of cells from the artery at either end of the graft. This method is worthy of more serious study and further application in man.

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Resectional Surgery of the Abdominal Aorta

Problems of Case Selection and Operative Technique

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Direct surgical attack by resection and grafting has earned a lasting place in the treatment of aneurysmal and insidious obliterative diseases of the abdominal aorta. As this method of therapy, in the wake of the many reported excellent early results,* becomes more popular, an assessment of certain problems concerning operative indications and technical steps in its use appears desirable. Among many such problems the most vexing ones in our experience have been the determination of the operability of aneurysmal lesions (by operability here being meant not merely technical resectability but resectability with a "reasonable" hope of cure) and the selection of the appropriate excisional procedure for obliterative disease. We wish, therefore, to present the lessons we learned in attempting to cope with these problems in the management of 15 aneurysmal and 19 occlusive aortic lesions treated by resection and grafting.

ANEURYSMAL DISEASE: OPERATIVE INDICATIONS AND CONTRAINDICATIONS

The true scope of resectional therapy in the treatment of abdominal aortic aneurysm is difficult to define for several reasons. First, the information concerning the natural history of the untreated aortic lesion is scanty. Secondly, the average mortality rate of the operation in hands of adequate but not exceptional competence is not yet known, since all our important statistics have come from two vascular centers of uncommonly large experience.† Finally, the determination of the presence of cure in successfully resected cases will not be possible until several more years of postoperative observation have elapsed. Obviously, the correlation of the information relating to all these three factors would be needed for an exact statement of the scope of applicability of resectional therapy. While such a definitive statement must wait for the accumulation of further experience, it is even at present possible to formulate useful standards of guidance in case selection by means of analyzing the available statistical information regarding the behavior of untreated aneurysms of the abdominal aorta and the observations so far afforded by operative experience.

Statistics of the Intrinsic Lethality of Abdominal Aortic Aneurysm.—The first factor with bearing on the extent to which resectional surgery may be applied in the treatment of abdominal aortic aneurysms is the lethality of the aortic lesion, that is, the rate of frequency with which such an aneurysm, if untreated, kills the patient that bears it. Clear-cut statistical information in this respect is difficult to find, since during the past two decades there has been a major shift in the relative and absolute incidence of syphilitic and thoracic aneurysms, on the one hand, and arteriosclerotic and abdominal aortic aneurysms, on the other. Since the early 1930's most statistics show a marked relative and absolute increase in the frequency of arteriosclerotic aneurysms at the expense of syphilitic aneurysms.[21] In a parallel manner the frequency of abdominal aortic aneurysms has risen and that of thoracic aortic aneurysms has declined. The older statistics,

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* References 1 to 20.

† References 3 to 11.

moreover, were influenced by the type of hospital population from which they were derived, big-city institutions and institutions with a high proportion of Negro patients furnishing high rates of incidence of syphilitic aneurysms. These features of the available statistical information can be illustrated by the following figures given together with the name of the author, the year of publication, and the place of origin of the report: Kampmeier [22] (1936), Baltimore, 68 cases of abdominal aortic aneurysm, with an incidence of syphilitic origin of 57%; Mills [23] (1938), Rochester, Minn., 26 cases, 8.0%; Hubeny [24] (1940), Chicago, 48 cases, 75.0%; Scott [25] (1944), Baltimore, 62 cases, 74%; Zech and Merendino [26] (1954), Seattle, 51 cases, 0.0%, and Maniglia [21] (1954), Philadelphia, 31 cases, 4.0%. Since the anatomic and pathologic characteristics of abdominal aortic aneurysms due, respectively, to arteriosclerosis and syphilis are significantly different, many of the reported figures are unsuited for common statistical treatment. Owing to this fact and since the abdominal aortic aneurysms seen in most large clinics at present are almost without exception arteriosclerotic, it is necessary to limit the analysis of mortality figures to those reports that refer entirely or preponderantly to aneurysms of arteriosclerotic origin. This precaution, unfortunately, reduces considerably the available data. Another necessary step in analyzing the statistical figures is the elimination of those reports that contain data referring to both thoracic and abdominal aneurysms without an anatomical breakdown of the information [27] or comprise data based on insecure diagnostic criteria,[28] further diminishing the extent of the statistical material. While the data left at one's disposal after the enforcement of these restrictions are not abundant, they show such definite trends as to permit certain conclusions. First, it appears clear that abdominal aneurysm is a highly lethal disease. The proportion of patients with abdominal aortic aneurysm who succumbed to the direct effects of this lesion was found to be 63.3% by Estes,[29] 65.2% by Nixon,[30] and 41.0% by Zech and Merendino.[26] In our own series of 38 cases, 61.6% of the patients died as the direct result of their abdominal aortic aneurysm. A second and corollary fact is that among those patients who do not die of their aneurysmal lesions a very large fraction fall prey to some other deadly manifestation of the pathological process underlying their aneurysms, namely, arteriosclerosis. Among our own patients 26% died of such causes, or about two-thirds of those who had not succumbed to their aneurysms. The experiences of others recorded in recent reports are similar.[26] A third conclusion can de derived from a comparative evaluation of the mortality figures for symptomatic and asymptomic aneurysms, which reveals that symptomatic aneurysms have a much higher mortality rate than asymptomatic aneurysms.‡ In our group of patients with abdominal aortic aneurysms the rate of mortality directly attributable to the aneurysm was almost three times higher among patients with symptoms than among patients free from symptoms. In the report by Zech and Merendino [26] this ratio was nearly two to one.

The conclusions just enumerated have direct though varying significance as regards the scope of surgical therapy. A lesion with such dismal outlook as abdominal aortic aneurysm has must be approached aggressively, and a considerable degree of risk may be taken in this approach. At the present state of our experience it would be unrealistic to estimate just how high a mortality rate would be acceptable in view of the great degree of lethality of abdominal aortic aneurysm. The generally accepted premise seems to have been that all such lesions, whether symptomatic or asymptomatic, should be treated by direct surgery, irrespective of the operative risk. It would seem reasonable, however, not to lose sight of the other two conclusions derived from statistical considera-

‡ It should be noted that by symptom due to an abdominal aneurysm we do not mean the discomfort of varying degrees caused by the size and pulsation of the vascular swelling but rather the pain, constant and typical in character, brought on by the slow perforation ("leakage") of the aneurysmal sac.

tions and listed above. Of particular significance is the fact that a very considerable portion of the patients with abdominal aortic aneurysms will die before their normally expected span of life is reached of the effects of the basic disease (i. e., atherosclerosis), regardless of the results of the surgical treatment of their aneurysms. The prognostic implications of the third statement deduced from the statistical studies, that is, the importance of symptoms, will be discussed presently.

Technical Difficulties as a Factor in Operative Mortality.—Practically all abdominal aortic aneurysms encountered in present-day practice are resectable in the purely technical sense. Size in itself is of very little significance in the task of performing the resection. Upward extension to or above the level of the renal arteries is generally considered an absolute technical contraindication, but in some instances even this barrier will in time be overcome. In any case, however, at most 10 to 15% of all lesions encroach on the renal arteries. There are, however, great variations in the magnitude of the technical problems the surgeon must deal with in technically resectable cases, and their importance is particularly decisive, since the patients are invariably impaired and often very poor risks. The extent to which the difficulties influence the mortality rate is, of course, to

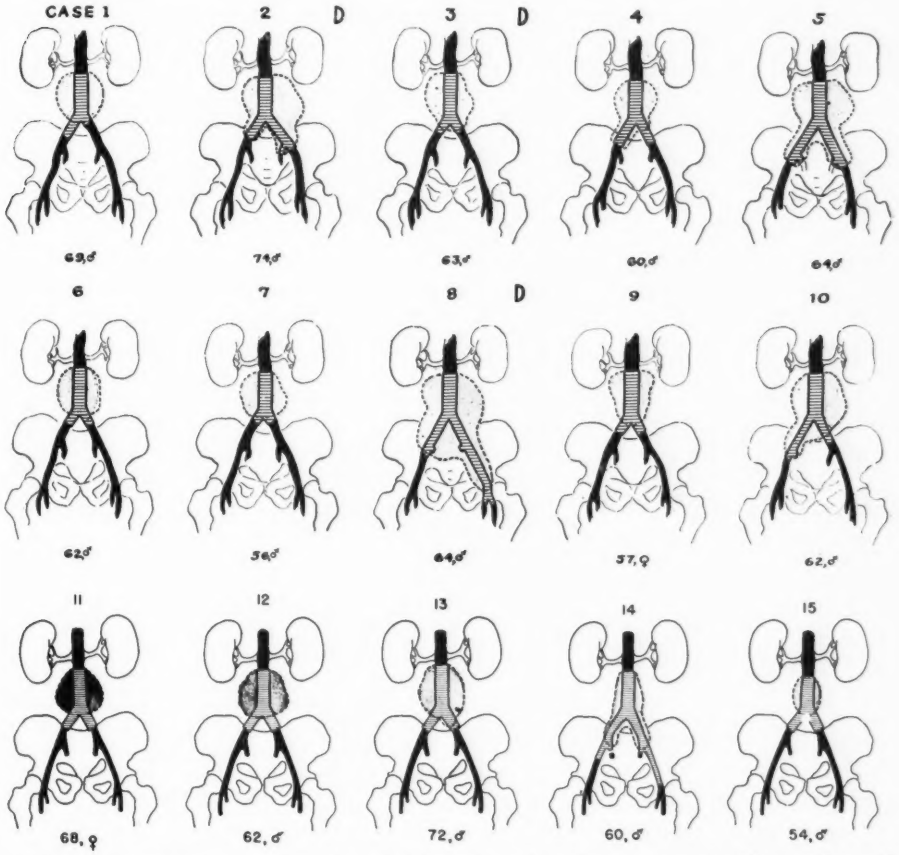


Fig. 1.—Disposition and configuration of abdominal aortic aneurysms treated with resection and grafting. The cross-hatched areas represent the segments replaced by homografts. (D means operative death. The serial case numbers correspond to those in Table 2.)

a significant degree dependent on the technical skill and experience of the operator—factors that are subjective and therefore difficult to project into a critical analysis. In discussing these factors we have in mind, of course, our own experience, which has been rather modest, and, if the operative competence was at times less than necessary to meet the demands made on it, the conclusions reached may be short of the truth; whatever error is committed thereby, however, it will be on the side of caution and the lesson will be all the more instructive.

Some of the remarks that follow will be better understood if first a brief description of the operative plan pursued in the cases is given.

After the necessary exploration of the aneurysm to determine its resectability, the upper level of resection is defined by freeing completely the infrarenal aorta lying proximal to the aneurysm. The distal level of resection is next determined by dissecting out the iliac arterial systems until segments of artery are reached that show structures suitable for anastomosis. In order to allow speedy and safe mobilization of the aneurysm, and also in order to prevent embolization while the aneurysm is being mobilized, the freed segment of the aorta as well as those of the iliac vessels chosen for anastomosis are clamped. In this manner the entire dissection of the diseased vascular segment—the aorta and the diseased iliac trunks—is carried out with the aortic blood flow occluded. The length of the time of occlusion of the aorta undoubtedly has an important bearing on the work-load of the heart, since some elevation of the blood pressure invariably ensues upon clamping the aorta, the elevation at times being as much as 100 mm. Hg or more. On the other hand, occlusion of the aorta even for prolonged periods of time at the level

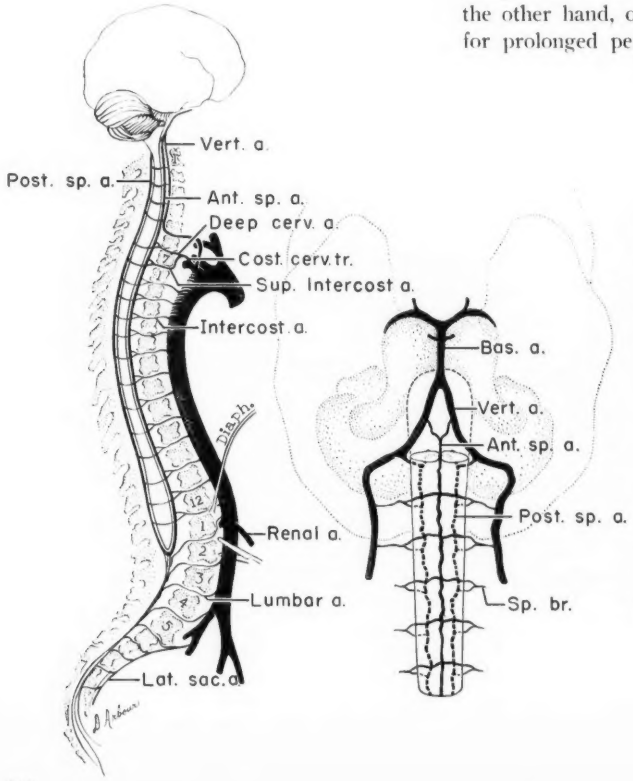


Fig. 2.—Blood supply of the spinal cord. Occlusion of the aorta by clamping distal to the renal arteries will cause no interference with the vasculature of the cord proper; the blood flow to the cauda equina will be reduced but this structure tolerates partial ischemia well.

Abbreviations: *post. sp. a.*, posterior spinal artery; *vert.*, vertebral; *ant. sp.*, anterior spinal; *cerv.*, cervical; *cost.-cerv. tr.*, costocervical trunk; *sup. intercost.*, superior intercostal; *lat. sacr.*, lateral sacral; *bas.*, basilar; *br.*, branch.

required for resection of infrarenal aneurysms causes no spinal cord damage, since the reduction of blood flow affects only the cauda equina, which tolerates the temporary ischemia quite well [Fig. 2]). Any technical difficulty that prolongs the time of dissection, and thus the length of occlusion of the aorta, will aggravate the hemodynamic changes consequent on aortic occlusion. Aside from these hemodynamic disturbances, however, excessive prolongation of the anesthesia, of handling, and of dissection is obviously detrimental in this as in other operations. The commonest factors causing delay are the adherence of the aneurysm to the vena cava and the iliac veins and the presence of aneurysmal involvement of the iliac vessels, the latter requiring wide dissection that must extend deep into the pelvis and even into the thigh. The first of these technical hardships can largely be overcome by leaving the adherent parts of the aneurysmal sac in situ, but the effects of the second, the extension of the disease into the iliac arteries, cannot be completely evaded. By tying both internal iliac arteries, the number of anastomoses and thus the operative time could be reduced, but this is an unsafe practice; we observed two instances in which temporary occlusion of both iliac arteries (in presence of the previous ligation of the inferior mesenteric artery) led to severe ischemia of the rectosigmoid colon (Fig. 3).

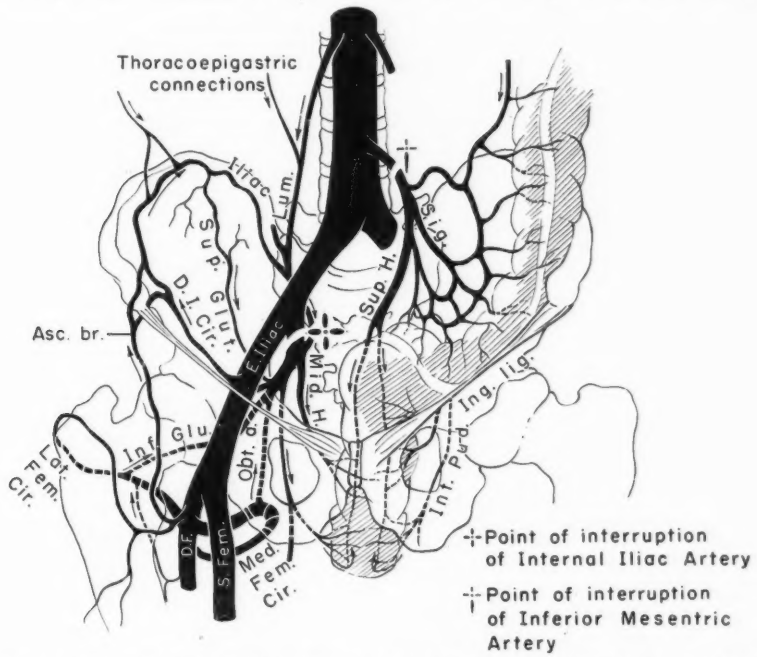
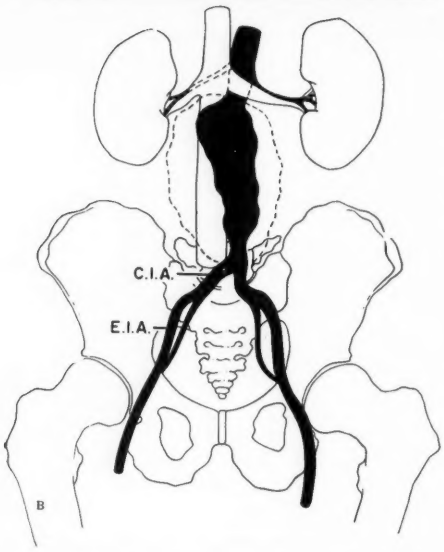


Fig. 3.—The collateral arterial pathways after simultaneous interruption of the inferior mesenteric and both internal iliac arteries. The blood supply of the rectosigmoid colon is seriously impaired, and ischemic necrosis is likely to supervene unless added collateral pathways are available either owing to anatomical variations or as the result of the stimulus of some insidious arterial obliterative process. The latter condition usually obtains in segmental occlusive disease but it may not be present in cases of aneurysm.

In all three elective aortic resections ending fatally in this series (Table 3) the cause of death was operative shock (irreversible hypotension), which, in turn, was the direct result of excessively long operative time occasioned by the technical difficulties briefly listed above. At autopsy in all three cases the technical result was excellent in terms of intact graft and suture lines. All three pa-

Fig. 4.—An example of the help one may derive from aortography in surgery of abdominal aortic aneurysms. In this instance (Case 9, Table 2) the aortograms showed a relatively normal segment of aorta, quite adequate for anastomosis, between the renal arteries and the aneurysm (left). On routine exploration the aneurysm was found to extend much closer to the renal arteries than anticipated (right). Only after complete freeing of the left renal vein, lying over the topmost portion of the aneurysm, and of the renal arteries did it become evident that the lesion was resectable. Without the clear-cut angiographic proof of operability one would most likely not have undertaken the extensive and difficult mobilization of the renal vessels but, on the findings of routine exploration, would have pronounced the aneurysm nonresectable.



tients had had severe coronary arteriosclerosis (two patients having had previous coronary infarcts), but no recent coronary thrombosis could be demonstrated at autopsy.

Until a careful review of the circumstances of death had been made in these three fatal cases, we followed the criterion that all patients bearing an aortic aneurysm, irrespective of the presence or absence of symptoms, should be offered surgical treatment. The lessons of these cases have led us to the conclusion that the technical difficulties of a proposed aortic resection are one of the factors to be weighed in determining operability. The significance of the technical problems must be evaluated, of course, in conjunction with certain other factors, as will be presently seen.

Unfortunately, technical problems in a given case often cannot be assessed until a fairly thorough surgical exploration has been done. In some cases, however, aortograms can supply helpful information both as to the relationships of the renal vessels to the aneurysm (Fig. 4) and with respect to the distal extension of the aneurysmal changes (Fig. 5).

The Consideration of the Permanence of Operative Results.—The question whether the successful resection of an abdominal aortic aneurysm is truly curative is pertinent in judging the scope of resectional therapy. Among the various subsidiary problems involved in the answer to this question only one can be clarified with certainty at this time; we know that by successfully removing an aneurysm we have eliminated a lesion of a high degree of lethality. We do not yet know, however, what the fate of the graft will be, nor can we predict the future behavior of the aorta proximal to the graft or that of the large pelvic arteries that so often show extensive disease. Admittedly, however,

Fig. 5.—Preoperative aortogram showing extensive aneurysmal involvement of the iliac arteries, a finding that always portends added technical difficulties (Case 5, Table 2).

these uncertainties must not weigh heavily in the balance; we must accept them as inevitable shortcomings of an operation that at the moment is the most satisfactory treatment we can offer. A much more important aspect of the problem is the fact that patients with abdominal aortic aneurysms are affected with a systemic disease of which the aneurysm is only one, albeit a most serious, manifestation. This systemic disease at the present time is in almost every instance arteriosclerosis. Obviously the progression of this incurable disease is not affected by the excision of the aneurysm. It is certain that in some cases the evolution of the systemic disease will lead to death before the span of normal life expectancy is completed. How greatly this turn of events will reduce the survival rate of the patients with resection we will not know with any degree of accuracy until the postoperative observations have extended over a period of time long enough to cover the range of life expectancies. One can make some estimates, however, on the basis of the mortality statistics of untreated cases of aneurysm and the life expectancy tables of clinically manifest forms of arteriosclerosis. In our own experience (Table 2), covering 38 untreated proved abdominal aortic aneurysms, 70% of the patients had significant arteriosclerotic disease of various types; 40% had arteriosclerotic heart disease, and 27% died of manifestations of arteriosclerosis other than their aneurysm, mostly of coronary occlusion (15%). The statistical data of other observers are similar.[26] In accordance with these figures, if we operate on every case of abdominal aneurysm, about one-fourth of all the patients will probably not be saved by their operation from death due to their basic disease. Moreover, the mortality rates of patients with clinically manifest coronary, cerebral, or renal arteriosclerosis are three times that of the corresponding age groups of the general population.[31] Properly speaking, therefore, patients having these forms of arteriosclerosis in combination with their aneurysm have no hope of cure by aortic resection but rather only palliation. Indeed, deaths in the early postoperative period caused by atherosclerotic (usually coronary) disease have already been observed (Table 3).

The Factor of Age.—Age has two limiting effects on the scope of resectional therapy. With the advance of years the general atherosclerotic process is more marked and its

TABLE 1.—*Abdominal Aortic Aneurysm, Clinical Material*

Lesions diagnosed (1920-1954)	93
Lesions proved (by angiography, operation, or autopsy)	53
Proved lesions treated with resection and grafting*	15
Proved lesions not treated with resection and grafting†	38

* Operative mortality 3/15 or 20%.
† Including four cases of rupture operated on in extremis.

TABLE 2.—*Survival in Thirty-Eight Cases of Untreated Proved Abdominal Aortic Aneurysms*

	Cases, No.
Died of aneurysm	24
Died of other forms of arteriosclerosis	10
Died of causes other than arteriosclerosis	3
Living	1
	38

The interval between diagnosis and death varied from less than one day to five years. The only living patient has been under observation for six years since her aneurysm was first diagnosed.

influence on the operative risk greater. Among the published reports the effect of age on the mortality rate is striking; in one very large series[7] the operative mortality for ages 70 to 79 was double that for ages 60 to 69. Moreover, it is obvious that the patient of advanced years has less extension of his life to be expected from the operation. Past 75 years of age the life expectancy of patients is probably only slightly lowered by the presence of an untreated abdominal aortic aneurysm.

Summary of Factors in Case Selection.—Several circumstances can be cited as urging an aggressive approach to the surgical treatment of abdominal aortic aneurysm. In a purely technical sense, 90% or more of these lesions can be treated with resection and grafting. Abdominal aortic aneurysms are highly lethal, causing by rupture the ultimate death of about 60% of the patients afflicted with them. There is no clinical sign or test that would accurately predict which ones of these lesions will rupture and when. Yet with asymptomatic abdominal aneurysm certain considerations counsel selection in advising excisional surgical treatment, an operation that carries a mortality rate of about 20% even in the most experienced hands,[7] and probably a higher rate for the less expert surgeon. From clinical observation, as well as from reflections on the known behavior of untreated abdominal aortic aneurysms and arteriosclerotic disease as mirrored in statistical studies, it seems that the careful balancing of the predictable operative technical difficulties with the cardiovascular status and age of the patient (most simply expressed as operative risk) will result in the selection of patients with the lowest at-

TABLE 3.—*Clinical Characteristics of Fifteen Cases of Abdominal Aortic Aneurysms Treated with Resection and Grafting*

Case No.	Age	Sex	Symptom Referable to Aneurysm*	Associated Disease†	Result	Follow-Up, Mo.	Comments
1	69	M	Absent	.....	Good	30	.....
2	74	M	Absent	.....	Post-operative death in 13 hr.	..	Early ischemic necrosis of rectosigmoid colon found at autopsy (see also text)
3	63	M	Present	Arterial hypertension; hypertensive and arteriosclerotic heart disease; previous coronary occlusion	Post-operative death in 24 hr.	..	See text
4	60	M	Present	Arteriosclerotic heart disease; previous coronary occlusion	Good	1½	Sudden death from coronary occlusion (no autopsy)
5	64	M	Present	Arteriosclerotic heart disease	Good	15	Appearance of aneurysm at site of intimectomy in right external iliac and common femoral arteries at 5 mo. postoperatively
6	62	M	Present	.....	Good	12	.....
7	56	M	Present	Arteriosclerotic heart disease; previous coronary occlusions	Good	10	Coronary occlusion 48 hr. postoperatively with good recovery
8	64	M	Absent	.....	Post-operative death in 48 hr.	..	Enormously large aneurysm requiring resection of both iliac systems as far as upper thigh (see also text)
9	57	F	Absent	Arterial hypertension (200/110)	Good	8	.....
10	62	M	Absent	Arteriosclerotic heart disease; previous coronary occlusion	Good	8	Appearance or reticulum-cell sarcoma at 5 mo. post-operatively, responding well to irradiation with radio-cobalt
11	69	F	Absent	.....	Good	5	.....
12	62	M	Absent	Pulmonary emphysema; chronic bronchitis	Good	4	.....
13	73	M	Absent	.....	Good	4	.....
14	60	M	Present	.....	Good	4	.....
15	54	M	Absent	8 yr. postoperative resection of carcinoma of sigmoid colon	Good	2	.....

* The symptom here referred to and regarded as significant is the severe boring pain in the lumbar, lumbosacral, or pelvic regions and at times radiating into the upper thigh or testicle.

† All patients had some degree of systemic arteriosclerosis. Notation is made here only of clinically evident organic manifestations of this disease.

tainable mortality rate and with the most lasting postoperative benefit. The technical hardships often cannot be estimated without surgical exploration, but in many cases preoperative aortograms may furnish helpful information, especially as regards the state of the iliac arteries. With respect to the contraindications that systemic arteriosclerosis may impose on the surgeon, a recent (less than three months old) coronary infarct, any evidence of congestive cardiac failure, moderate or marked renal insufficiency, and cerebrospinal vascular lesions should disqualify a patient for resectional treatment.

The criteria of operability are quite different in cases of symptomatic or ruptured aneurysms. As mentioned above, slow perferation (dissection or leakage) causes severe boring and often radiating pain in the low back and pelvic region. These lesions have a mortality rate almost twice that of asymptomatic aneurysms and should be operated on regardless of the restrictive criteria listed for asymptomatic aneurysms.

When the aneurysm has ruptured, surgical intervention is likewise mandatory unless there is previous knowledge that the aneurysm is technically unresectable or unless the patient's condition prohibits the administration of an anesthetic agent. These cases are absolute surgical emergencies.

As to the procedure of choice in the cases of patients who by these standards are found inoperable, we doubt that the older forms of conservative surgical treatment (wiring and wrapping) have enough to offer to warrant their use in place or resectional therapy. We have found it a practical and fairly safe plan to instruct the patient unsuited for elective surgery about the danger of rupture or dissection and in particular about the significance of the character and intensity of the pain he may experience and advise him to seek immediate medical care upon the ap-

TABLE 4.—*Clinical Characteristics of Nineteen Cases of Aortoiliac Segmental Occlusion Treated with Resection and Grafting*

Case No.	Age	Sex	Palpable Pulses in Lower Limbs	Associated Disease	Result*	Follow-Up, Mo.	Comment
1	48	M	None	.....	Good	24	.....
2	52	M	None	Arteriosclerotic heart disease; coronary insufficiency	Good	18	Coronary occlusion 12 mo. postoperatively
3	54	M	Questionable right femoral	Arterial hypertension; arteriosclerotic encephalopathy (early)	Good	17	.....
4	57	M	Questionable left femoral	.....	Good	14	.....
5	45	M	All on right	.....	Partially good	13	Right common iliac anastomosis thrombosed
6	51	M	Questionable right femoral	.....	Good	13	.....
7	61	M	None	.....	Good	11	.....
8	52	M	Questionable right femoral	.....	Good	11	.....
9	59	F	None	Nontoxic nodular goiter	Good	10	.....
10	57	M	Right femoral	Advanced systemic arteriosclerosis	Bad	..	Operative death (see text)
11	59	M	All on left	Arteriosclerotic nephropathy (early)	Good	8	.....
12	48	M	None	.....	Partially good	8	Right common iliac anastomosis thrombosed
13	65	M	Questionable left femoral	Arteriosclerotic-cardiopathy (early)	Good	6	.....
14	55	M	None	Arteriosclerotic cardiopathy; previous coronary occlusions	Partially good	6	Left common iliac anastomosis thrombosed
15	61	M	None	.....	Good	5	.....
16	53	F	Left femoral	Recurrent mechanical small bowel obstruction (postoperative adhesions)	Good	1	Intestinal obstruction with peritonitis 5 wk. postoperatively; death
17	63	M	Questionable left femoral	Arteriosclerotic cardiopathy; earlier coronary occlusion	Bad	..	Operative death (see text)
18	49	M	All on right	Arteriosclerotic cardiopathy (early)	Good	2	.....
19	49	M	All on right	.....	Good	1	.....

* For criteria of classification of results see Footnote to Table 5.

TABLE 5.—*Results of Resection for Aortoiliac Segmental Occlusive Disease*

	No. Operated On	Results		
		Good	Partially Good*	Bad†
"Pure" segmental occlusion (S. O.)	17	14	3	0
Diffuse arteriosclerosis with S. O.	2	0	0	2

* Good results mean relief of symptoms, return of previously absent pulses, and patent graft by angiography. In the cases with "partially good" results one iliac anastomosis became clotted and on the corresponding side the limb remained unchanged; otherwise the operation was successful.

† Operative deaths

pearance of pain. In almost all cases of rupture, death is far from instantaneous and, if time is not wasted, there is a better than fair opportunity for removal of the aneurysm.

SOME TECHNICAL PROBLEMS IN THE TREATMENT BY RESECTION AND GRAFTING OF AORTOILIAC SEGMENTAL OCCLUSION

Though some division of opinion still exists concerning the respective positions of resectional therapy ‡ and thromboendarteriectomy § as the preferable form of treatment for insidious obliterations of the aortoiliac segment (Leriche's syndrome), in our opinion excision with grafting has by far the greater intrinsic merits. In what follows we wish to describe some of the technical problems we have encountered in the use of this type of therapy and the manner in which we attempted to solve them (Tables 4 and 5 and Fig. 6).

Pure Segmental Occlusion and Segmental Occlusion with Diffuse Arteriosclerosis.—Most writers regard all aortoiliac segmental occlusions as allied manifestations of the protean disease of arteriosclerosis. Unquestionably the microscopic pathologic appearances of the surgical and autopsy specimens of the affected arteries do not justify any etiologic subdivision; the changes seen are, however, the nonspecific scars of old, unidentifiable insults, and thus they are difficult to interpret in terms of the etiologic factors that result in the pathologic picture designated as arteriosclerosis. In any case, whether due to qualitative or quantitative differences, on the clinical plane two fairly distinct classes of the lesion can be recognized. One form, which one may call pure segmental occlusion, is characterized by fairly sharp limitation of the occlusive changes to the aortoiliac area, with appreciably, often strikingly, less involvement of the distal arterial bed. In the other form, which may be designated as diffuse arteriosclerosis with segmental occlusion, the obliterative changes extend (without perceptible transition) into the distal arterial bed. Microscopically, as formerly mentioned, no clear distinction between the two types can be made. Grossly the so-called pure form tends to show more periarterial fibrosis, less tendency for aneurysmal dilatations, and less calcification; the obliterative process is preponderantly an intimal proliferation rather than a thrombosis. In the diffuse type the gross alterations are chiefly those of medial necrosis often with sacciform dilatation of the wall, intimal atheromatosis and, as the final phase of occlusion, intraluminal thrombosis. The gross characteristics are of great significance from the therapeutic point of view, since they largely predetermine the suitability of these lesions for surgical therapy. For both technical and general physiological reasons resection with grafting is especially practicable and efficacious in dealing with so-called pure segmental occlusion. It is almost always possible to find distal arterial segments with relatively slight arteriosclerotic changes and thus with walls that allow easy anastomosis. The distal arterial bed being, as a rule, ample and open, and thus the flow of the blood through the graft free, the maintenance of a patent graft is more likely. Since the ample collateral circulation is usually adequate to assure viability of the extremity even if the graft fails to remain open, there is very little likelihood of worsening the condition of the affected limb after an unsuccessful or partially successful operation. In most instances the atherosclerotic involvement of the remainder of the cardiovascular system is of a lower degree, and, thus, the operative risk is smaller. All these conditions are reversed in diffuse ar-

‡ References 6, 7, 12, 13, and 16.

§ References 32 to 37.

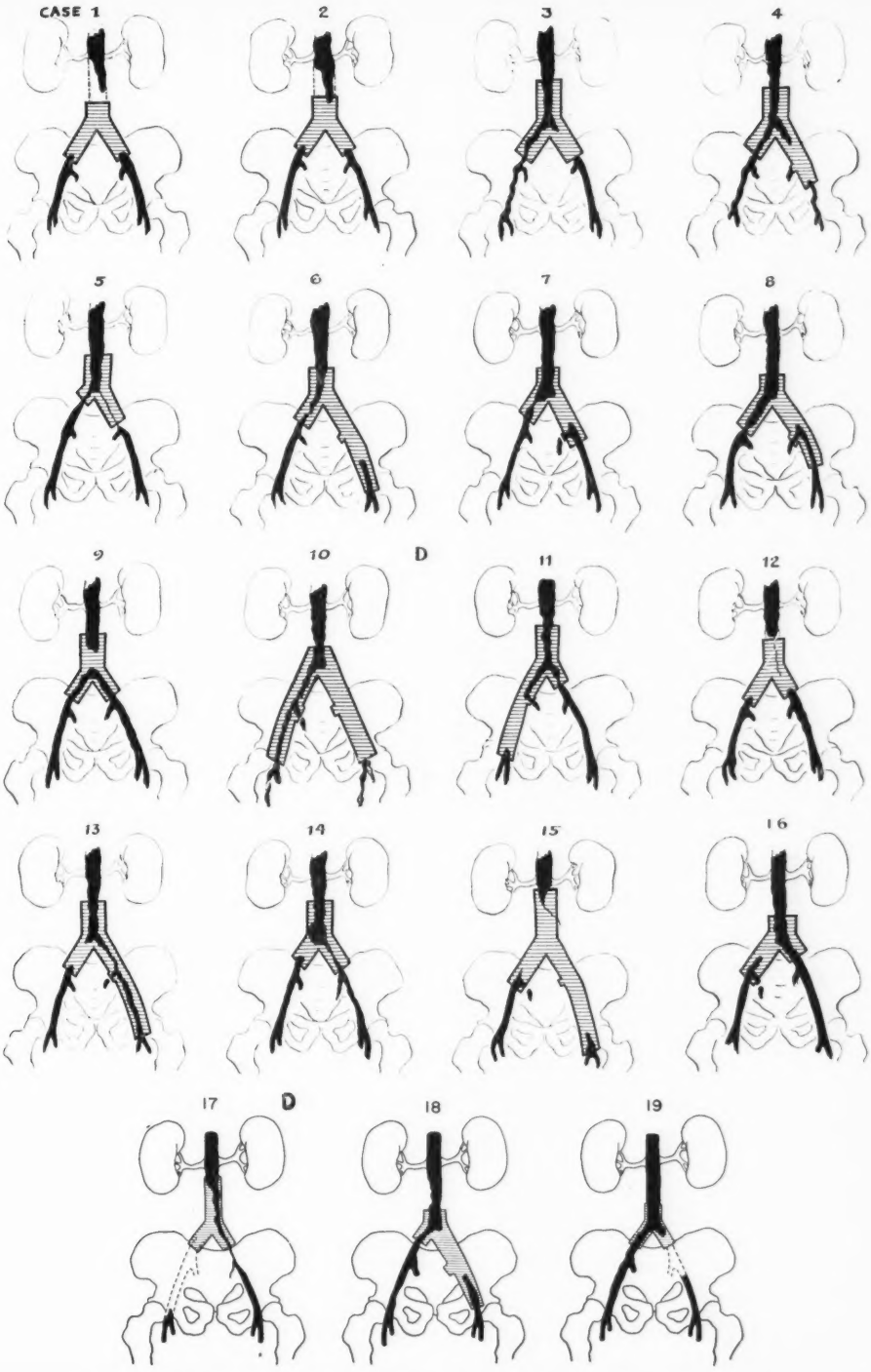


Fig. 6.—Disposition and configuration of the aortoiliac occlusive lesions. The cross-hatched areas represent the segments replaced by homografts. (D means operative death. The serial case numbers correspond to those in Table 3.)

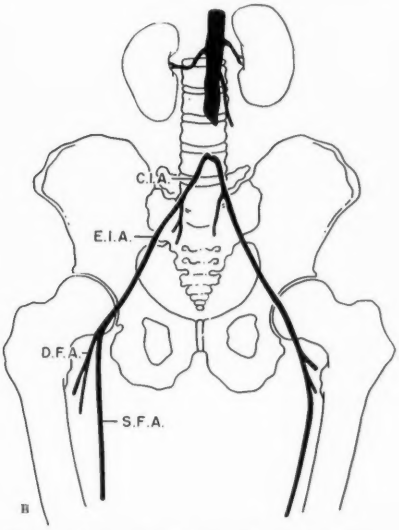


Fig. 7.—Aortogram in case of so-called pure segmental aortoiliac occlusion (Case 9, Table 3). The disease is largely limited to the aortic bifurcation and the adjacent common iliac arteries. The neighboring arterial bed is free from significant atherosclerotic changes.

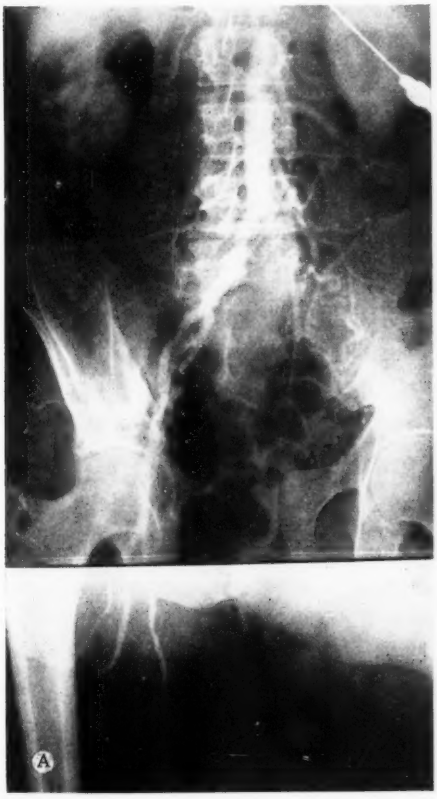
teriosclerosis with segmental occlusion. As a consequence, in the cases of the latter type resection and grafting are technically more difficult, the fate of the graft less secure, and postoperative complications resulting in loss of limb or even life more likely to take place.

There are clinical findings that help in differentiating the two classes of patients, but an accurate distinction can be made only by angiography (Figs. 7 and 8). On the clinical plane, the patients with pure segmental occlusion are about 10 years younger and manifest few evidences of systemic arteriosclerosis; their outstanding complaint is exertional pain (intermittent claudication) with no important signs of ischemia at rest. Since the differences both pathologically and clinically are quantitative rather than qualitative, the clinical manifestations may overlap, and thus the differential diagnosis by clinical means alone may be impossible. Angiographic studies in such instances are of great help, and they assist not only in establishing the essential character of the lesion but also in determining the general plan of surgical intervention by delineating the exact area of obliteration as well as the collateral circulation.

Among the 19 aortoiliac segmental occlusions we have had the opportunity of treating with resection and grafting, 2 were examples of diffuse arteriosclerosis and 17 were of the so-called pure type. Six patients of the latter group showed a significant amount of systemic arteriosclerosis, and thus their classification may be questioned; the distal iliac and femoral arterial beds in these cases, however, revealed an appreciable freedom from sclerotic changes.

It may be added in passing that there was another group, of five patients, classified as examples of diffuse arteriosclerosis that were

treated with thromboendarteriectomy. All the patients so treated required emergency operations for early or impending gangrene of the lower limbs supervening on a sudden complete thrombosis of the partially occluded aortoiliac area, and they all died postoperatively. They all had autopsy examinations and showed far-advanced diffuse arteriosclerosis of the aortoiliofemoral arterial bed. The fate of this group must not, of course, be interpreted as a fair test of the general usefulness of thromboendarteriectomy, since these patients were all desperately, even hopelessly, ill before they were operated on. They exemplify, rather, the possible doleful consequences of partial aortoiliac obliteration secondary to diffuse arteriosclerosis, in which, because of the lack of adequate collateral arterial bed, sudden terminal thrombosis results in ischemia of the gravest type.



In the group with resection and grafting there were two operative deaths and both occurred in cases of diffuse arteriosclerosis. In one instance (Case 10 in Table 3) the cause of death was irreversible operative shock brought about by an exceptionally long and complicated surgical procedure necessitated by technical difficulties. In the other case (Case 17 in Table 3) death was due to intractable congestive cardiac failure with acute pulmonary edema.

Among the 17 cases of pure segmental occlusion good results (return of previously absent pulses, angiographically patent graft, and complete relief of symptoms) were obtained in 14. In three cases one of the iliac anastomoses failed to remain patent; these patients experienced complete relief on the successful side but remained unchanged on the other. The causes of these partial failures will be further discussed below.

These experiences corroborate the assumption, based on the pathological characteristics of the lesion, that aortoiliac segmental occlusion superimposed on diffuse arteriosclerosis is poorly suited for resectional surgical treat-

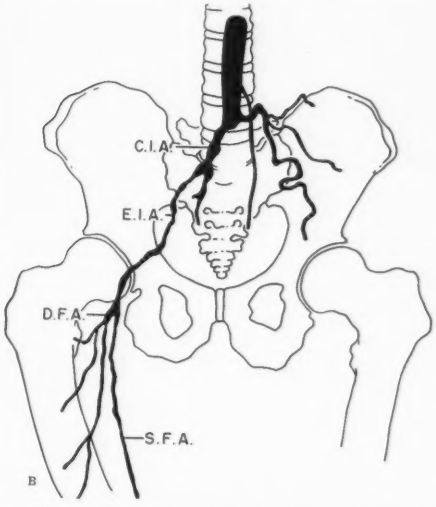


Fig. 8.—Aortogram in case of segmental aortoiliac occlusion secondary to diffuse arteriosclerosis (Case 10, Table 3). The iliac arterial systems are extensively diseased bilaterally. The changes extend to the right femoral system as well; on the left no patent distal femoral stump is visualized (although one was demonstrated at operation).

ment. The results obtained by others with resection and grafting in similar cases have likewise been unsatisfactory.[5] Whether thromboendarteriectomy would be more successful in such cases is a question to which our experience cannot give an answer, since, as already stated, the patients for whom it was tried were in hopeless straits. In more favorable cases this type of surgical therapy would undoubtedly yield better results. Conservative surgery limited to sympathectomy, as recommended by others, could in some instances be beneficial. We have found that bypassing grafting procedures || without resection gives excellent early results in selected cases of this type, but our experience has as yet been too small and too recent to allow a positive judgment of their value.

The Problem of the Extent of Resection in Incomplete Aortoiliac Segmental Occlusion.—In this series incomplete occlusion of the aortoiliac segment was frequent (Fig. 6). By aortography one of the common iliac arteries was shown to be partially patent in 12 of the 17 cases of so-called pure segmental obliteration. On grounds of both the clinical symptoms and absent or questionable femoral pulsations in 6 of these 12 cases, the clinical diagnosis of complete bilateral iliac occlusion was made. Indeed, even at exploration it was impossible to demonstrate with certainty the patency of the partially occluded segment by palpation alone, and without a knowledge of the angiographic appearances these lesions might easily have passed scrutiny as examples of complete aortoiliac obliteration. We believe that in cases of this type the resection of the aortic bifurcation and the diseased lengths of both common and external iliac arteries—in other words, their management as if occlusion were bilaterally complete—is for several reasons the correct procedure. Technically the resection of only one common iliac artery would be hard and risky, in fact often impossible, because of the difficulty of establishing a satisfactory anastomosis between the graft and the severely diseased aorta. It is, moreover, highly probable that the disease already deep-seated in the partly occluded iliac branch is progressive. We have not had the opportunity of actually observing the evolution of this process to the point of complete obliteration in pure segmental occlusion but have seen complete occlusion supervene with disastrous effects on earlier partial occlusion in cases where the basic pathological picture was that of diffuse arteriosclerosis. (The progressive character of the pathologic process renders the use of bypassing grafting procedures ill-advised in these situations.)

The decisive point of information in such instances is the degree of involvement, usually well represented in aortograms and confirmed by exploration. One may thus find that the disease involving the common iliac artery may be limited enough to allow the partial resection of this artery. In cases such as portrayed in this study with advanced, even though unilaterally incomplete, segmental occlusion, complete graft replacement seems to be the suitable operative procedure.

The Management of the Distal Arterial Stumps.—The segmental character of the aortoiliac obliterative process is a relative one. The pathological changes seldom come to an abrupt end but rather fade away by stages. In the understandable endeavor to avoid the lengthening of operative time by the need of making triple or quadruple distal anastomoses and the placing of excessively long grafts, one's tendency is to spare as much of the distal iliac arterial trunk as seems practicable. As a consequence one is often tempted to make the distal anastomoses across common iliac arteries that still show intimal disease. In such contingencies our practice for some time was to carry out an intimectomy on the distal arterial end. This was done in six cases involving 11 iliac arteries. By removing the diseased intimal and medial layers with a sharp and smooth breakoff point, it was possible to secure satisfactory stumps for anastomosis in most cases.

|| In operations of this kind the involved segment is undisturbed, and a shunt is made around it by means of a graft anastomosed to the aorta above and a suitable patent vessel distally; the anastomoses are usually end-to-side (end of graft to side of host artery).

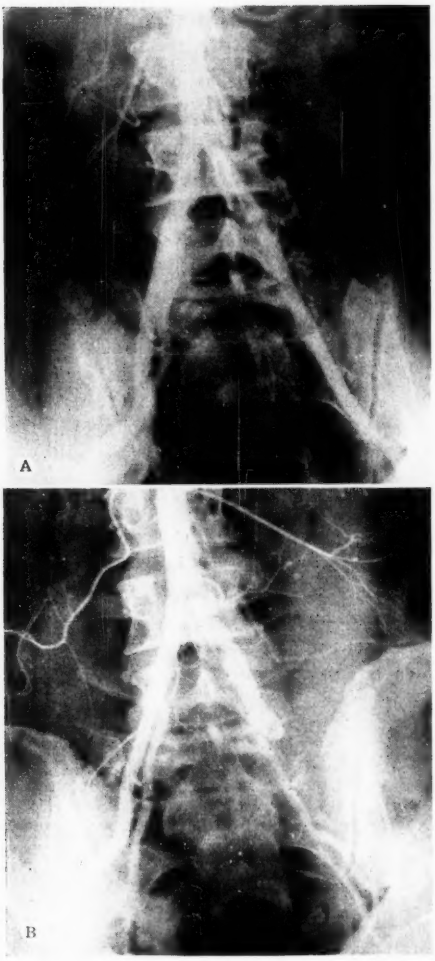
In three instances (involving four iliac arteries) among the six in which intimectomy was performed, however, the distal anastomosis became occluded within the first few postoperative hours (Table 3). The cause of these unhappy complications was undoubtedly the infolding of the loose edge of the intima as it became undermined by the blood stream at the distal limit of the intimectomy. This explanation is not only an inference from the appraisal of the anatomical relationships but also the result of actual observations during the exploration undertaken to relieve the occlusion in two of the three cases as well as in another similar case where the primary lesion was an aortic aneurysm (Table 2, Case 5). Moreover, in a case of resection and grafting of the left common iliac artery, we had occasion to demonstrate angiographically the effects of this behavior of the intima (Fig. 9). By extending the intimectomy, at a considerable risk to the patient, into the femoral region in one of the three cases of obliterative disease as well as in the case of aneurysm, the intimal block could be relieved. In the other two cases of obliterative disease the secondary intimal occlusion could not be corrected. Thus, failure to maintain patency in the area of intimectomy was the cause of the unsatisfactory results in two of the three cases of aortoiliac resection in which one iliac anastomosis became occluded. In the third such case with unsatisfactory result on one side, the line of anastomosis apparently closed because of the presence of extensive arteriosclerotic disease in the wall of the distal stump used for anastomosis.

These observations suggest that the practice of performing an intimectomy on the diseased distal arterial end seriously endangers the future patency of the anastomosis and is undesirable except under the most favorable circumstances. Rather than resort to intimectomy or use arterial stumps of questionable quality for anastomosis at the common iliac level, we prefer at present to carry the resection of the arterial trunk as far distally as necessary in order to come upon reasonably sound arterial wall to suture. We have found that the pathological changes of the arterial wall in cases without diffuse arteriosclerosis diminish significantly as one reaches the external iliac artery, and in the common femoral trunk they are usually of such slight degree as to allow good anastomosis without intimectomy. (This is, emphatically, not the case with diffuse arteriosclerotic occlusion.) In seven cases we extended the dissection in this manner into the upper femoral region and found the suturing of the graft to the common femoral artery just proximal to the bifurcation an easy and successful task (Cases 4, 6, 8, 11, 13, 15, and 18, Fig. 6). The anatomical details of the approach to the external iliac artery are illustrated in Figure 10.

It may be briefly added that the technical management of the distal arterial stump is an equally important problem in the excisional therapy of abdominal aortic aneurysm. The preferable way of dealing with the problem is probably the same as outlined above, although the task of coping with it is harder, since the anatomopathologic conditions are often different, owing to the greater degree of diffuse arteriosclerosis present. In one case of abdominal aortic aneurysm we attempted to solve the problem of distal anastomosis by performing a very extensive intimectomy, the distal limit of which was at the femoral bifurcation. This patient eventually developed an ileofemoral aneurysm in the site of intimectomy which had to be resected and grafted (Case 5, Table 2). An important difference between the cases of aneurysm and cases of occlusive disease with regard to the problem of extending the length of resection must be stressed. Whereas in occlusive disease, especially if the aortoiliac obliteration is complete, simultaneous ligation of the inferior mesenteric artery and both internal iliac arteries can be done with complete impunity; in aneurysmal disease it is usually necessary to preserve the patency of one internal iliac artery.

SUMMARY

With the background of the clinical study of 53 abdominal aortic aneurysms and the experience of 34 resections of lesions of the abdominal aorta (15 aneurysms and 19 aor-



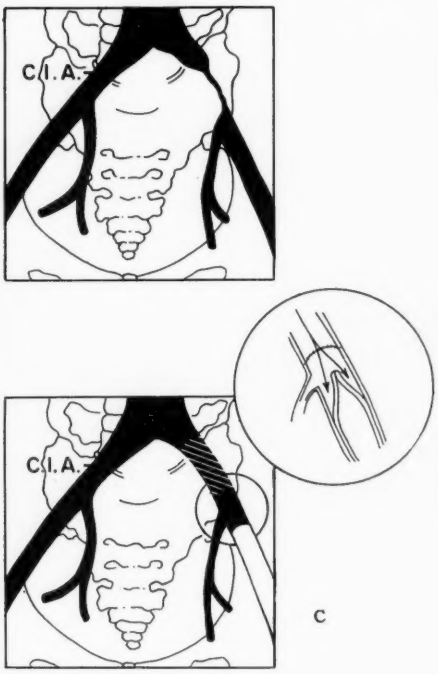


Fig. 9.—Complication of intimectomy (thromboendarteriectomy). A short segment of incomplete occlusion of the left common femoral artery (top left and right) was resected and replaced by a homograft. The postoperative angiograms (bottom left and right) showed that the graft (seen as a cross-hatched area) and a segment of the common iliac artery (including the portion giving off the internal iliac artery) remained patent, but the external iliac artery became occluded at a point corresponding to the distal limit of the operative intimectomy that had been carried out preparatory to the insertion of the graft. The obvious conclusion is that at that point the intima became folded in (inset) and acted as a ball valve. (Abbreviation: *C.I.A.*, common iliac artery.)

toiliac segmental occlusions), the problems of aneurysmal case selection and some technical questions in the resectional surgery of the abdominal aorta are discussed. Certain criteria of operability are suggested in the management of abdominal aortic aneurysm. The prognostic significance of the distinction between pure segmental aortoiliac occlusion and segmental aortoiliac occlusion secondary to diffuse arteriosclerosis is stressed. Resection of the entire aortic bifurcation and of all the diseased portions of the common iliac arteries is advised for the treatment of incomplete but advanced aortoiliac occlusion. An extension of the level of resection distalward is recommended in preference to intimectomy in cases where the degree of arterial disease does not permit anastomosis with the intact artery at the common iliac level.

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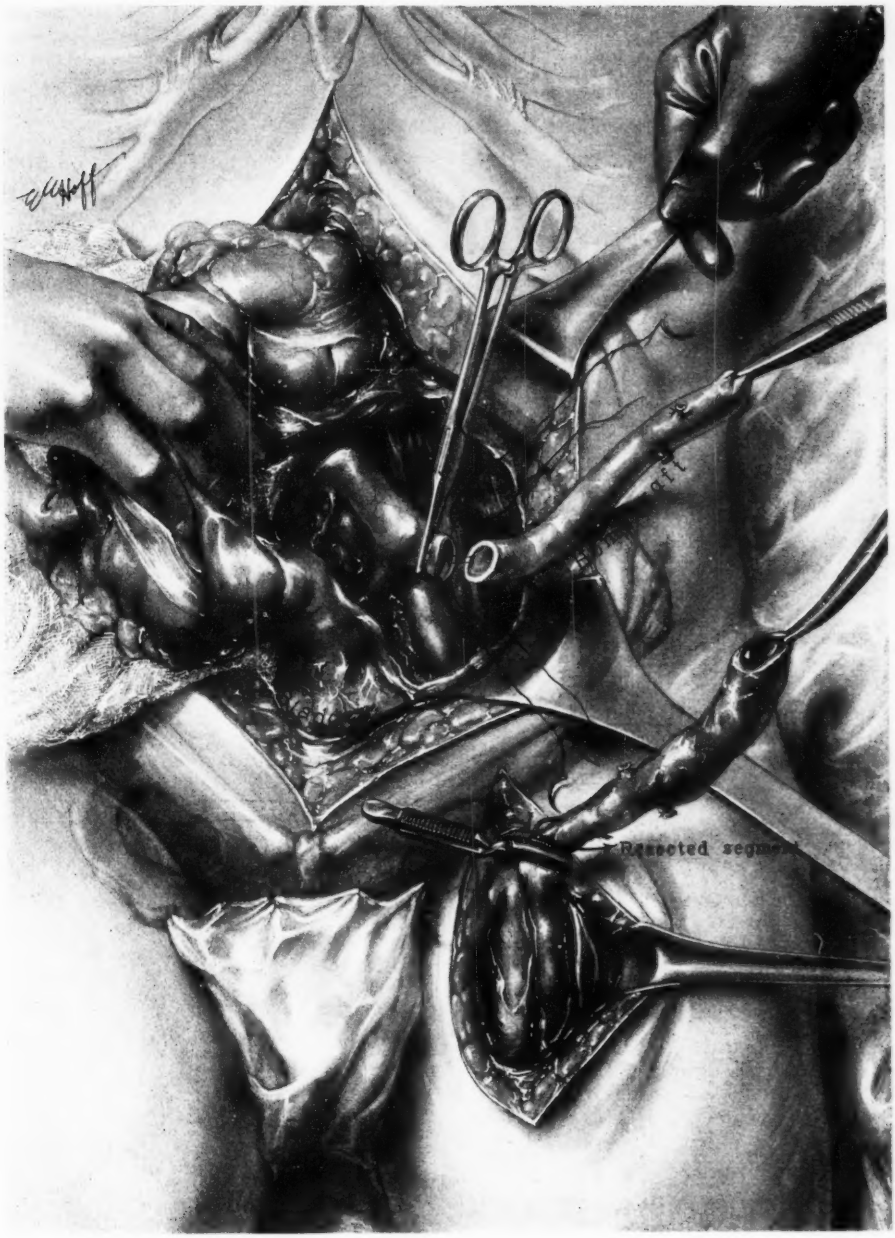

Fig. 10.—Combined abdominal and femoral approach to the resection of the left external iliac artery. (The approach on the right is the same in principle and differs only in some anatomical details.) This operative step is incorporated, on one side or both, into the procedure of resection of the aortic bifurcation and common iliac arteries whenever the extent of the pathological changes require excision of the external iliac and common femoral arteries as well.

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DISCUSSION

ON PAPERS BY DRS. E. J. HARRIS, H. B. SHUMACHER, J. H. SIDNEY, T. C. MOORE AND P. F. GRICE; L. G. HERRMANN AND C. G. BOLLACK; D. E. SZILAGYI, P. R. OVERHULSE, AND R. F. SMITH.

DR. HAROLD LAUFMAN, Chicago: Dr. Shumacker has asked me to discuss the paper by Dr. Harris and his group. I will limit my remarks to that paper, because our interest has been mainly experimental.

Despite the enthusiasm from various quarters throughout the country, I do not believe the ideal artificial arterial material has yet been found. We have used various materials in the laboratory, dating from our own interest in impervious materials, and then found out the hard way that they had to be pervious.

The one we have had most experience with is a material called Fortisan cloth, which is a pure cellulose fabric. I do not believe the type of fabric, be it cellulose or one of the nylon acetates, is of as much basic importance as are other factors about the material, such as softness, ease of wrinkling, elasticity, and other physical properties.

Dr. Shumacker was good enough to send us some of his nylon material. We find it is not only the material that is important. In the thorax, where most dogs of normal size have an aorta of 1 cm. or more, most grafts will stay patent. In the abdominal aorta, however, where the aorta may be 5 to 6 mm., no more than 50% of grafts, regardless of the material used, stay patent. They stay patent for five, six, or eight days and then become occluded partially or completely with thrombosis.

For this reason I do not believe the ideal material has yet been found, because in order to use synthetic materials for the spectacular kind of small vessel substitution (considering the femoral artery a "small" vessel) as Dr. Szilagyi has so beautifully done, so far the only successful material that can be used is actual homograft material.

There is no known artificial material in our experience which will remain patent in more than 50% of the cases with a diameter under 1 cm., and I think this is the reason why the human aortic implants in general have done better than the animal aortic implants.

DR. ORMAND C. JULIAN, Chicago: Dr. Szilagyi has given me the privilege of discussing this paper.

First, I think I should like to mention how curious it is, or perhaps how expected it is, that the problems arising in all investigators' series are just about the same.

We, like Dr. Szilagyi, have continued to use homografts rather than prostheses, although we look forward to a change.

A word about the indications for surgery in abdominal aneurysm. Dr. Szilagyi has shown some healthy conservatism. I agree with him in this except for one or two facts.

One of them is that in our series of resections of aneurysms of the abdominal aorta there have been four done for acute ruptures. These acute ruptures have occurred in asymptomatic aneurysms. This is a very significant point, showing that there may not be any warning symptoms.

The statistics presented by Dr. Szilagyi of prior papers, particularly those of Estes, showing the grave prognosis of symptomatic aneurysms, is another point in favor of resection of symptomatic aneurysms. My point of the four ruptures in asymptomatic aneurysms is a point in favor of the resection of all aneurysms.

We have been paying attention to one point having to do with resection of obliterative lesions of the distal aorta, especially in those which occur in diffuse arteriosclerosis. The preoperative aortogram frequently does not show what the distal artery is like and particularly if it does not refill well through the collateral system. In these cases we have done open femoral arteriography to supplement the aortogram.

To prevent dissection of intima distal to the distal anastomosis after surgery, we have avoided in recent cases doing any intimectomy distally. Rather, we have sutured even fairly bad arteries when we are faced with the need, leaving all coats of the vessel in place, being careful to place the needle from the lumen side out in the diseased segment, adequately suturing down the intima, and preventing the dissection produced by the flow of blood over the suture line later.

DR. JOSEPHUS C. LUKE, Montreal, Canada: In discussing Dr. Szilagyi's paper I should like to confine my remarks to those cases of arteriosclerosis obliterans of major vessels and to emphasize the point he has made in case selection.

This procedure is a new one, which at present is being performed by a few vascular surgeons. However, it soon will be in the realm of general

surgeons, and the number of cases recognized will increase. The results obtained, however, will depend on two factors: technical skill and, mainly, case selection. Cases with diffuse arteriosclerotic disease along with a segmental occlusion should be ruled out, as should those with multiple areas of segmental occlusion. It has been our experience that persons over 60, and sometimes those much younger, are seldom suitable for this operation. Anyone starting in this field of surgery should select as his first few cases those in the 40's or 50's who have a segmental occlusion of a major artery of external iliac artery size or larger and whose proximal and distal vessels are shown by arteriography to be not much involved by arteriosclerotic disease.

In the management of such a case, we operate with a suitable homograft on hand. The occluded artery is opened to determine if the case is appropriate for thromboendarterectomy. If suitable, this operation is preferred to that of resection and grafting. Last year before this Society we gave our results with this technique, and the subsequent year has confirmed our opinion that this procedure gives good results, is easier and more physiological than grafting. If the arterial wall reveals extensive plaque formation, or if the intima is extensively degenerated or thickened, then resection and grafting is preferable.

Dr. Edgar S. Brintnall, Iowa City: I will confine my remarks to only one matter.

When thromboendarterectomy (intimectomy) is indicated, either alone or as an adjunct to arterial transplantation procedures, the problem of terminating the procedure arises. Care must be taken to prevent intimal curling or elevation at the level at which the intimectomy is ended. Mattress sutures through the vessel wall are not effective in preventing intimal dissection and thrombosis and do not provide a smooth vessel lining. Hence, thrombotic occlusion commonly occurs.

In our experience this problem has been solved simply by deliberately cutting across the artery at the level at which it is desired to terminate the intimectomy. An end-to-end anastomosis is then set up between intimectomized vessel above and nonintimectomized vessel below. The anastomosis everts intima, provides a smooth lining for the artery, and prevents thrombosis at this level.

Dr. Robert N. Watman, Columbus, Ohio: I think Dr. Herrmann makes the point very well that arterial prostheses serve as scaffoldings for the growth of host tissue, so that the final product is an autologous vessel rather than homologous or heterologous.

Following the principles he has so nicely stated, we have attempted the use of nylon-wrapped and -supported homologous veins as arterial replacements. We have the feeling that they should be readily and easily obtained, that the limitations of atherosclerosis, older age, and so on, would not be a significantly limiting feature. The nylon support should prevent the inevitable aneurysmal dilatation that one sees in veins placed in large arteries, and perhaps human tissue would be the best possible scaffolding for humans and dog tissue for dogs in the experimental laboratory.

[Slide] This is one of our finished grafts. As you can see, a venacaval graft taken from a donor animal has been placed into the abdominal aorta and wrapped with a rather coarse nylon mesh. In wrapping, the mesh is so placed as to constrict the graft down to aortic size to make a generally cylindrical, uniform vessel.

[Slide] In a significant number of our animals, not in all but in some, we found quite early ulcerative degenerative intimal changes. This represents an early ulcerative degenerative case. In the favorable case there is replacement, but in the unfavorable case ulceration progresses.

[Slide] This shows moderate ulceration.

[Slide] This shows extensive ulceration with exposure of the nylon supporting net.

[Slide] Finally, between the 5th and 6th months, somewhere around the 21st to the 24th week, a significant number thrombosed and became completely occluded. We were rather pessimistic about that. I take some heart from the fact that one of the commentators mentioned that the general results show about 50% occlusion in any type of graft in the abdominal aorta of the dog. That is about what we got—50% successful and 50% occluded, apparently by the mechanism just illustrated.

At this time it would seem that, in spite of all the reasons for undertaking these venous grafts, the inert prostheses appear to be more successful than the technique we have explored.

I should like to thank Dr. Herrmann for this opportunity to discuss his paper.

Dr. James E. Conley, Milwaukee: I should like to comment on just one aspect of Dr. Szilagyi's paper and that is in regard to the use of serial x-ray films when one is doing aortography. It may add additional help in selecting patients for surgery. Aortography is not an innocuous procedure; so any additional help obtained in regard to the arteries distal to the occlusion may be of assistance in selecting patients for surgery.

[Slide] This aortogram was taken in series of 0.5-second intervals with a total of 2 seconds between these films. It shows the occluded site, and after two seconds we see a very satisfactory filling of both iliac arteries up to the bifurcation. This is true segmental occlusion, and it was confirmed in the lateral spine x-ray, which showed the small area of calcification.

[Slide] This shows a similar area of occlusion. Serial films were taken and failed to show any

evidence of filling of the iliac arteries at two seconds.

The two patients whose aortograms were shown were approximately the same age, but clinically they represented different types of disease. This second case had a diffuse type of vascular disorder. Both extremities were quite cold, and there was dependent rubor, with slow filling of the veins on the dorsum of the feet on dependency, while the first case had very satisfactory filling of the veins on dependency, no dependent rubor, and no atrophy of the muscles or the skin, presenting clinically a segmental occlusion.

Dr. E. J. Harris, Indianapolis: I wish to thank Dr. Laufman for his discussion of our paper. In regard to thrombosis in plastic grafts of small size, I feel it is worth while to emphasize that in using grafts of nylon filter fabric with a diameter of 0.78 cm. we encountered only one occluding thrombus in 19 cases.

Dr. Shumacker has used with success for aortic and aortic bifurcation replacement grafts of fused nylon and polyethylene and grafts made of nylon filter fabric.

Dr. Louis G. Herrmann, Cincinnati: I should like to reemphasize what Dr. Laufman has alluded to in his discussion of this problem, namely, that the wholly ideal material for bridging defects in major arteries is not yet available. Chemists are constantly developing synthetic fibers of various kinds and of various chemical compositions, and it seems logical that our specifications for a substitute for human elastic tissue will be met eventually. It is true that cloth or tubes made of the various synthetic fibers that are now available from the chemists can be used to bridge gaps in large arteries satisfactorily, but we must strive to make available for clinical use a product which will be accurately standardized in its manufacture and which will be inert when implanted into the human body. The commercially available plastic cloths vary widely in their purity and the residual content of the plasticizers used in their manufacture. This may account for the varied reactions of human tissues to some of these synthetic materials.

It is our opinion that the ingrowth of fibroblasts from the periarterial and retroperitoneal tissues through the synthetic elastic framework of the prosthesis is of the greatest importance, for this is then the basis for true arteriogenesis.

Dr. D. Emerick Szilagyi, Detroit: I wish to thank Drs. Laufman, Julian, Luke, and Conley for their very interesting remarks.

With respect to Dr. Julian's comments, it is indeed correct that I speak in favor of the conservatism of selectivity insofar as asymptomatic abdominal aortic aneurysms are concerned. When an aneurysm gives rise to symptoms, however, the situation one faces is different. If, on a careful evaluation, the symptoms are those of dissection or, as is commonly called, "leakage," operative treatment is imperative, regardless of the presence of other atherosclerotic manifestations or even of a recent coronary infarct, as was the case with the patient described in one of our slides. The same holds true for ruptured aneurysms.

The point I wish to emphasize is that in the management of asymptomatic lesions the problem of operative indication is one of balance, the balance between the operative risk and the benefit one may expect from the operation.

If I may be allowed to appear in the double capacity of closing a discussion and also making a comment on a previous paper, I should like to bring up two points about plastic arterial protheses. First, without wishing to detract from the great potential value of plastic cloths, I should like to state that homografts are still the best arterial substitutes. The search for plastic replacements has been stimulated mainly by the scarcity of human vascular material. I should like to advance the proposition that it is possible to maintain an adequate supply of human arterial homografts in any general hospital of 200 beds or over with an autopsy incidence of at least 50%. Time is too short to discuss any details, but it can be briefly said that a solvent artery bank can be maintained in such an institution if the following three requirements are met: (1) A thorough indoctrination of the house staff regarding the importance of obtaining, together with the authorization for autopsy, permits for the donation of tissue for grafting; (2) a simple and safe method of sterilizing vascular grafts that will allow their procurement under routine autopsy conditions (we have found β-propiolactone very satisfactory for this purpose), and (3) a method of preservation allowing long-term storage of the graft, the best being lyophilization.

The second point I wish to mention about plastics is that the shortcoming of plastic prostheses that to me appears the most disturbing has not been adequately investigated, namely, the problem of the lack of elasticity. Most of the experimental work has concerned itself with the replacement of broad and short aortic segments, and in such replacements most types of prosthesis will give a fair degree of success. In replacing arterial segments 20 cm. or more in length and 10 mm. or less in width, the elastic quality of the prosthesis becomes important. From animal experiments it would seem to us that in the replacement of long and narrow arterial segments the lack of elasticity that characterizes all the plastic prostheses now available may be a disadvantage. There is a need for a type of plastic fiber with intrinsic elastic quality or a textile structure that lends the fabric at least a temporary elasticity.

Reactivation of Rheumatic Fever Following Mitral Commissurotomy

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and
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The medical literature in the past two to three years has contained articles concerned with the reactivation of rheumatic fever following mitral commissurotomy. It is the purpose of this paper to present the essential findings and conclusions following the study of 100 consecutive patients who received surgery for mitral stenosis in relation to the clinical and laboratory findings that might suggest reactivation of rheumatic fever. Of the 100 patients 4 might be considered as having reactivation of their rheumatic fever.

Preoperatively we attempt to have the patient free of active rheumatic fever and other nonrelated infections. We find that blood studies are important and helpful but not absolute. The sedimentation rate and antistreptolysin titer have been normal, yet the microscopic studies of the auricular appendage may reveal a marked rheumatic activity. The patient must be well compensated and the circulating blood cells within normal limits as to number and quality prior to surgery.

The patients are classified as to their cardiac status in the four groups that are used by most workers. We have not operated on a Group I patient; 5 Group II patients, 25 Group III and 70 Group IV were operated on. Of these 1 of Group III and 11 of Group IV died during their hospital periods.

A portion of the left auricular appendage in most cases is removed at surgery to allow the entrance of the operating finger. The histopathological studies of the appendages have been made and classified as to their cellular activity into the inactive, or the group showing no evidence of rheumatic heart disease, and the active group which shows definitely a rheumatic carditis (Figs. 1 and 2). Of the 88 auricular appendages studied 52% showed microscopically rheumatic activity in the endocardium and myocardium. All five of the patients 20 years and below showed microscopically rheumatic

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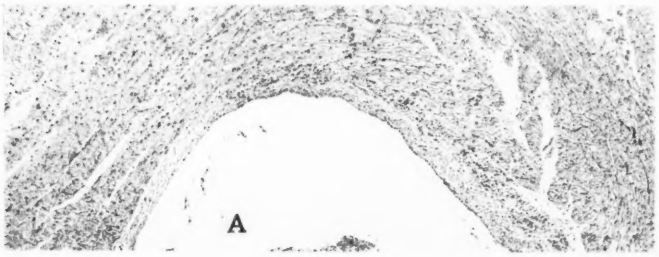

Fig. 1.—Low-power section of the amputated auricular appendage showing almost a continuous chain of typical Aschoff nodules in the subendocardium. This has been classified as active rheumatic carditis.

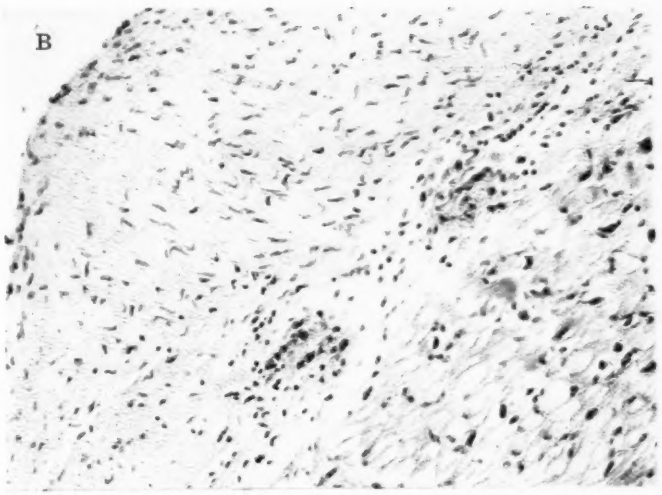

Fig. 2—High-power section showing two typical Aschoff nodules in the subendocardium revealing histocytes or "owl-eyed" cells with ragged-edged nuclei. They are basophilic-staining and are intermingled with eosinophilic-staining collagen material.

activity. Sixty-six per cent of the patients (18) between 21 and 30 years of age showed rheumatic fever activity by histological study. The patients between 31 and 40 years were divided equally, while the patients whose ages ranged from 41 to 50 years showed microscopically no presence of rheumatic heart disease in 66% of the 19 auricular appendages studied. Two patients, 51 years and 59 years of age, showed microscopically rheumatic activity, while six others in the same age group, or 75%, showed no inflammatory cellular activity in the auricular muscle.

These studies are interesting, informative, and stimulating.

REPORT OF CASES

The four patients that we are considering that may have had a reactivation of their rheumatic fever ranged in age from 12 to 25 years. All had, histologically, active rheumatic heart disease.

PATIENT 1.—This patient, a 25-year-old unmarried woman, was operated on four years ago. She had had rheumatic fever at the age of 14 years, exertional dyspnea and orthopnea for 11 years, and ankle edema for four to five months. Clinical findings were those of mitral stenosis. The electrocardiogram showed right ventricular hypertrophy and strain and an enlarged left atrium. The sedimentation tests prior to surgery were 18 mm. and 2 mm. per hour. Postoperatively the patient's temperature remained elevated to 100.6 F for nine days, and she complained of more weakness and precordial pain than was usually noted. Blood cultures grew no bacteria. She was discharged on the 14th postoperative day and has made very satisfactory recovery.

We do not know if this was a reactivation, but it may so be classified by some. Histologically there was evidence of active rheumatic heart disease. The reactivation, if present, was mild.

PATIENT 2.—The second patient was a 20-year-old housewife that had rheumatic fever at 14 years of age, and since the birth of a child two years prior to admission she had had repeated bouts of decompensation. When admitted to the hospital she was in decompensation. The greatly enlarged heart caused marked precordial pulsations, and it was fibrillating. The electrocardiogram showed a right axis deviation and a mixed strain. She had predominantly a mitral stenosis with some regurgitation and a minimal aortic regurgitation. There was a pleural friction rub in the left axillary region. The sedimentation rates were 30 mm. and 21 mm. per hour taken six days apart. She was placed on anticoagulants, digitalis, low-sodium diet, and diuretics and was asked to return to the hospital two months later. The pleural rub had disappeared, and the sedimentation rate had dropped to 6 mm. per hour at the second admission. She had very little cardiac reserve and was a seriously ill Group IV patient. At surgery stenosis with some regurgitation

was noted. The stenosis was relieved. The postcommissurotomy left intra-atrial pressure was reduced one-third of its precommissurotomy value. The atrial appendage showed microscopically active rheumatic endocarditis. Her postoperative temperature was elevated for four days but her clinical course very slowly improved, and she was discharged to her home 28 days after surgery. She was readmitted 10 months later in partial decompensation and with elevation of her sedimentation rate. On careful medical management, by Dr. Oglesby Paul, she has greatly improved.

We believe this patient has had active rheumatic fever since first seen, associated with multivalvular disease, mitral stenosis causing the greatest disability. Surgical convalescence was prolonged because of the existing rheumatic activity and limited myocardial reserve. However, the rheumatic activity may have been prolonged by the surgical intervention, which we believed at the time was advisable.

We believe the third patient had a reactivation of her rheumatic fever.

PATIENT 3.—This 20-year-old housewife had rheumatic fever at 16 years of age. She had had dyspnea and orthopnea for the past two years and hemoptysis on one occasion. The ankles had swollen in the past two months. Clinically she had mitral stenosis with minimal aortic regurgitation. The electrocardiogram showed a right axis deviation. The sedimentation rate was 14 mm. The left atrium and first portion of the pulmonary artery were enlarged on x-ray studies; the heart was otherwise of normal size. A week after her admission to the hospital a commissurotomy was performed on a valve tightly stenosed with fibrous tissue. The microscopic study of the auricular appendage revealed active rheumatic heart disease. Postoperatively she responded very well except for a temperature rise to 100.6 F up to the 12th day after surgery. She was discharged on the 18th postoperative day and readmitted 11 days later with a temperature of 103 F, pulse rate of 100, and pleuritic pain on the left side. The blood culture gave no growth, the sedimentation rate was 42 mm. per hour, and the white blood cells were 16,600 per cu. mm. The heart shadow was increased in all directions as compared with the preoperative films. The patient was treated with antibiotics and acetylsalicylic acid, and within 36 hours her temperature was normal. One week after admission she was discharged to her home using sulfadiazine 0.5 gm. b. i. d. and acetylsalicylic acid. She was observed carefully by her family physician, and when seen 11 months after surgery she had no complaints and her heart rate and size had returned to within normal limits.

This 20-year-old patient, having given a history of rheumatic fever three years prior to admission, might well be suspected of having rheumatic cellular activity present in the myocardium and endocardium. Clinically she did not present that picture, nor did any laboratory tests suggest it. The microscopic study of the auricular appendage revealed active rheumatic heart disease. Twenty-nine days following surgery and eleven days after discharge from the hospital she was readmitted with fever, pleuritic pain, increased size of the heart, and elevation of sedimentation rate and white blood cell count. This acute flare-up of clinical rheumatic fever followed mitral-valve surgery.

PATIENT 4.—No definite history of rheumatic fever or chorea could be obtained from this 12-year-old patient or her parents. During the past year increasing dyspnea had developed. In the past six months she had had sudden attacks of weakness and rapid heart action and had collapsed. Clinical findings were of a very tight mitral stenosis and of active rheumatic fever. The heart was enlarged. The first portion of the pulmonary artery was markedly increased. Blood cultures gave no growth. The sedimentation rate was 30 mm., and the streptolysin titer was within normal limits. She had 10 gm. of hemoglobin, 3,180,000 red blood cells, and normal white-blood-cell count. The electrocardiogram showed right ventricular and auricular hypertrophy. During the first three weeks that she was in the hospital she was observed, and treatment consisted of a low-sodium diet, bed rest, and sulfadiazine 0.5 gm. b. i. d. She lost 4 lb. of weight in the first four days. Her pulse rate varied from 125 to 75 per minute. It was believed by all that observed her that the stenotic mitral valve should be opened if this child was to have a chance for improvement.

At surgery the pressure in the left atrium and pulmonary artery was found to be very high. The mitral orifice was very small. The commissures were divided without difficulty. The atrial surface of the valves felt to the examining finger like smooth granulation tissue. The postcommissurotomy intra-atrial pressure was one-third of that taken prior to opening the valve, which was in the upper range of a normal pressure. The studies of the auricular appendage removed at surgery show active rheumatic myocarditis. The patient's temperature and pulse were normal after the 14th day following surgery.

This 12-year-old child received a mitral commissurotomy in the presence of what was believed to be an active rheumatic fever, as a lifesaving procedure. The microscopic study confirmed the clinical diagnosis of active rheumatic heart disease. Surgery confirmed the severity of the mitral stenosis and relieved the obstruction. This child is now under treatment for rheumatic heart disease at the Herrick House and is progressing satisfactorily.

COMMENT

Two patients, we believe, had active rheumatic fever at the time of surgery. The other two patients presented no clinical or laboratory signs of activity; one had a definite clinical reactivation of rheumatic heart diease.

The histopathological study of the auricular muscle makes one realize that reactivation could take place much more frequently than we have seen in the patients studied. Subclinical reactivation may have taken place and was not recognized.

Reactivation may have been present in patients with other complications, such as pulmonary emboli or phlebitis arising at the site of intravenous therapy, etc. We did not believe the patients having these other complications showed symptoms or findings of a reactivated rheumatic carditis, and, thus, they were not included in this study.

Finding that about 50% of the patients with mitral stenosis give no history of rheumatic fever or chorea and that over 50% of the patients with clinically inactive rheumatic fever show microscopically rheumatic heart disease reconfirms the fact that the disease is hazardous and unpredictable in most patients. Of the auricular appendages studied from patients below the age of 30 years, 73% showed active rheumatic heart disease histologically. In this age group are the four patients with reactivation that occurred in this series. With increasing age the incidence of microscopically active rheumatic heart disease diminished. It thus appears that the younger age group with mitral stenosis continues to have active rheumatic heart disease without clinical signs and is most vulnerable to reactivation. We believe the histopathological studies of the auricular appendages are important in helping to determine the long-term postoperative care.* An antibiotic or sulfonamide is given daily over periods of years to prevent infections and reactivation of rheumatic heart disease. We believe this has been of great help in preventing reactivations, but we have no way to prove this belief at the present time.

The two patients operated on during clinically active rheumatic fever show that definite benefit is derived by commissurotomy, if mitral stenosis is the predominating disabling pathology.

The four patients that showed signs of reactivation have been benefited by mitral commissurotomy.

SUMMARY AND CONCLUSIONS

One hundred patients with mitral stenosis subjected to mitral valve surgery presented the following results as related to reactivation of rheumatic heart disease.

1. Histological evidence of active rheumatic disease in the cardiac muscle removed at surgery was shown in 52%.

2. The histological evidence of rheumatic heart disease is commonest in the younger age group but is present in all ages.

3. There were three patients from 20 to 25 years of age that presented clinical signs of rheumatic reactivity following mitral valve surgery. A 12-year-old patient was operated on during a clinically active stage of rheumatic fever.

4. Reactivation of rheumatic heart disease varied in the four patients from a mild to an active clinical reaction associated with a prolonged convalescence. The histopathology of each showed active rheumatic carditis.

5. It is impossible to predict which patient will have a reactivation; thus we believe it

* Dr. Oglesby Paul, Cardiologist at the Presbyterian Hospital, and Dr. Robert Dillon, of Cardiovascular Physiology Department of Cook County Hospital, cared for these patients before and after surgery.

wise to advise prolonged antibiotic therapy or chemotherapy postoperatively to patients showing rheumatic heart disease histopathologically.

6. The four patients that had a reactivation of their rheumatic heart disease following surgery have benefited by commissurotomy.

DISCUSSION

DR. ORMAND JULIAN, Chicago: I should like to thank Dr. Helmen for inviting me to discuss his paper.

The closing remarks, in which Dr. Helmen considers the difficulty in making certain diagnosis clinically of a recurrence of rheumatic fever, are of the greatest importance. We have had 4 cases of polyarthritis in about 200 patients operated on for mitral stenosis. These patients had joint pain migrating from one joint to another, but only one had swelling. We think these cases are undoubtedly recurrences of rheumatic fever.

In addition, there have been 2 cases of subacute bacterial endocarditis in these 200 patients, and there have been 10 additional patients not having joint pain who had a very suspicious febrile course without any other explanation than the clinical one that they may have rheumatic fever.

We don't know what the underlying cause of the fever was in these patients, but, in addition to the explanations offered in the paper, I should like to offer also the explanation that the auricular stump, devitalized by constricting purse-string sutures, in necrosing may produce a point from which fever can arise—fever and even mediastinal pain.

To be sure, the present understanding that we have, that rheumatic fever is a chronic disease that cannot be depended upon ever to be completely healed, and the frequent finding of myositis in the specimens removed at the time of mitral commissurotomy will continue to worry us and will keep us sensitized to this problem of recurrences following surgery.

DR. CONRAD R. LAM, Detroit: I apologize for being on the platform for the second time, but I believe it was thought to be a good idea to add our series for purposes of averaging.

Our experience has been a little different in our series of almost 200 cases. We have not had anything that could be called a typical recurrence of rheumatic fever with joint involvement. We have had our share of this miserable condition called "postcommissurotomy syndrome." I am not sure what it is. It may be nonspecific.

If human experimentation were possible, I believe we would find that if the normal heart were opened and were treated more or less as we do our hearts with mitral stenosis, we might see some cases of febrile illness. We also see the same thing in cases of intracardiac surgery, such as the Brock operation. There is certainly some pericarditis.

We have had one definite case of valvulitis shown by autopsy, and that was in a person upon whom an inadequate commissurotomy had been done. I had been satisfied with a finger fracture. I should have used the knife. I should like to ask the closing author to state if he was completely satisfied with the commissurotomy that was done in the cases reported.

DR. E. H. FELL, Chicago: We wish to thank the discussers for their emphasizing important points concerning this subject.

The postcommissurotomy syndrome and reactivation of rheumatic fever have been described by some to be common. The purpose of this paper, we believe, is to show that reactivations are uncommon. We find it, however, a difficult problem to decide which patients had a reactivation.

In the four patients that we believe had a reactivation, only one had a clinical reactivation of rheumatic fever. The others had prolonged convalescence and more discomfort and weakness than is usually seen. The patient that had the clinical reactivation had enlargement of the heart as well as prolongation of convalescence and fever. The four have done very well, and their cardiac function has been improved following the cardiac surgery.

Regarding Dr. Lam's question as to whether or not the commissurotomies had been complete, we believe that all commissures were satisfactorily divided, some with the knife and some without. The most difficult one to divide was in the child of 12 years of age who had an active rheumatic fever, and commissurotomy was performed as a lifesaving procedure. The precommissurotomy intra-atrial pressure was 54 cm. of isotonic saline. It came down to 18 cm. of isotonic saline after commissurotomy.

We should encourage careful microscopic study of the cardiac muscle removed at surgery, and we wish to express our appreciation to the pathologists at the Presbyterian Hospital for assistance and council. We believe that these cases, particularly the younger age group, where 75% have histological evidence of active rheumatic carditis, should be followed for a period of years. Either an antibiotic or a sulfonamide is recommended to control infections or recurrences during this period of observation. We cannot prove that this is of any benefit but believe there is something to it.

Drs. Albert W. Schweitzer and Gordon F. Vawter, of the Pathology Department of the Presbyterian Hospital, assisted by studying the pathological material in these cases.

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The Noble Plication Operation for Chronic Recurring Intestinal Obstruction

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Adhesions causing intestinal obstruction have always presented one of the most difficult problems in surgery. Adhesions between adjacent loops of intestine and the parietal peritoneum are an almost invariable complication of abdominal surgery, but in the great majority of cases these produce no symptoms. However, in a small number of cases complications do arise in the form of recurring intestinal obstruction. Lysis of adhesions by surgery or by decompression by long tubes often is followed by only temporary relief. All too frequently the situation becomes progressively worse after successive laparotomies, and many of these patients finally present severe nutritional problems. A certain number become narcotic addicts in addition to their chronic invalidism, which often adds to the despair of the surgeon. Since 1949 an increasing number of articles have appeared in the surgical literature attesting to the fact that the plication procedure offers the only practical method available for use in cases of chronic recurring intestinal obstruction.

In spite of the many methods recommended for the prophylaxis and treatment of peritoneal adhesions, an almost hopeless attitude existed in surgical circles until 1949. In 1937 Noble [1] first published a report on his method of plication for adhesions affecting the small intestine. This method received little or no recognition in the surgical literature until 1949, when Lord, Howes, and Jolliffe [2] pointed out that Noble had made a real contribution and that the method had definite value. The basic idea of Noble's plication procedure is that, while adhesions cannot be prevented by lysis, they can be controlled without impairing the normal motility of the small intestine.

In general, we believe that the plication procedure will produce much better results if used in those cases where definite episodes of obstruction have taken place. Abdominal pain due to visceral traction or partial fixation by peritoneal adhesions is not a clear indication for the operation, since many of these patients are emotionally unstable and any treatment will, all too often, give poor results.

We have preferred to treat acute obstruction by conservative methods if possible and to plan the plication as a definitive procedure after adequate preparation of the patient. Many of these patients have moderate to severe nutritional deficiencies which should be corrected before surgical intervention. We have therefore elected in the majority of our cases to use tube feeding with liquefied whole food for at least five to seven days.* We have been impressed by the smoother convalescence when the preoperative nutritional lag is corrected in this manner.

A transverse abdominal incision just above the umbilicus has given satisfactory exposure, and the incidence of postoperative her-

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* References 3 and 4.

niation has been minimal. The omentum and entire jejunum and ileum are freed by sharp dissection. In some cases certain areas are so hopelessly damaged that it becomes imperative to remove the damaged intestine and restore continuity by end-to-end anastomosis. It is important to conserve as much intestine as possible, since some of these patients have had segments of bowel removed previously.

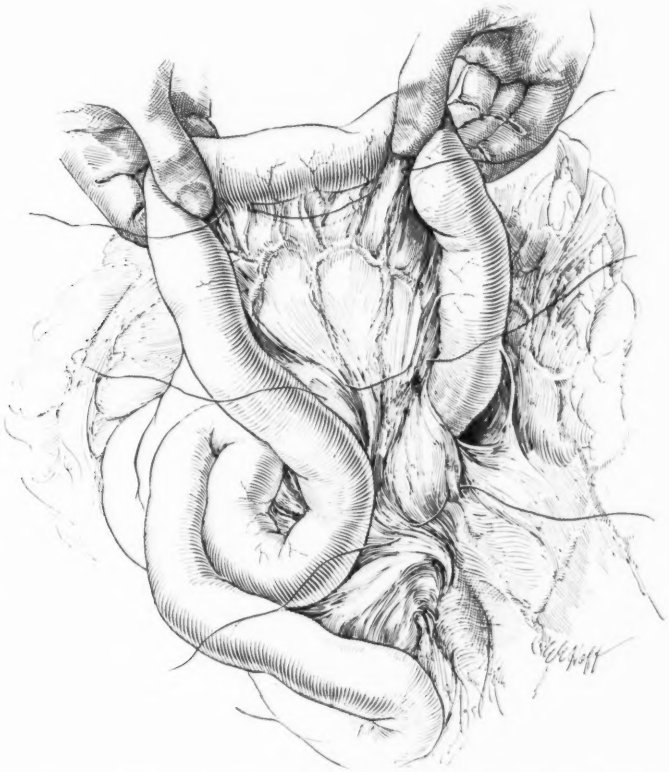

Fig. 1.—Three key sutures are placed as shown. The first is placed at the base of the mesentery. The other two sutures are placed in the mesentery near the intestine so that a triangle is formed with the apex at the base of the mesentery and the base at the junction of the mesentery and intestine. Interrupted fine silk sutures are then used to suture the area between the previously placed key sutures. Alternate sides of the mesentery are used as each loop is plicated.

The plication is started at either the lower ileum or the upper jejunum after complete freeing of these structures. Interrupted fine nonabsorbable surgical (silk) sutures on small French needles or straight intestinal needles are used to unite the mesenteric attachment of the intestinal loops, care being taken not to damage the blood supply. No sutures are placed in the bowel wall itself. In our experience the procedure has been greatly simplified by placing three key sutures at the start of each loop plication (Fig. 1). The first of these is placed near the base of the mesentery. The second and third are then placed in the mesentery near the bowel wall at each end of approximately 8 in. intestinal loops. This produces a triangular-shaped area, with the apex represented by the suture at the base of the mesentery. The

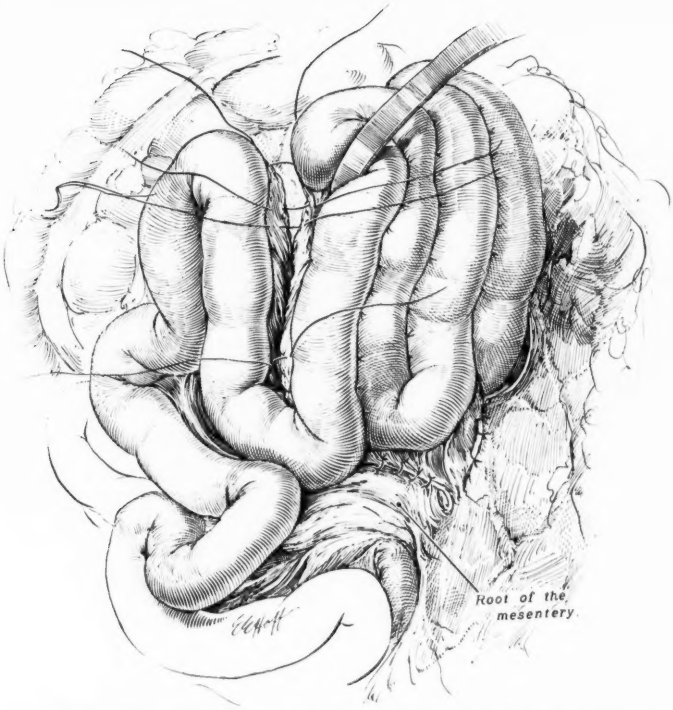

Fig. 2.—The plicated loops of bowel are about 7 to 8 in. in length. In severe cases the entire jejunum and ileum must be plicated. Note that plication is carried out on alternate sides of the mesentery.

mesentery then is approximated by interrupted sutures between the three key points. The same procedure is now carried out on the opposite side of the mesentery, the plication being repeated on alternate sides until the entire jejunum and ileum are plicated (Figs. 2 and 3). We are convinced that the entire jejunum and ileum must be plicated to obtain best results. The two failures in our series occurred in patients on whom only a limited plication was carried out. At reoperation the area that had been plicated was in excellent condition, but the portion of the bowel that formerly appeared in good condition was now involved. At the completion of the plication the omentum, when present, is placed between the incision site and the plicated small intestine.

Fig. 3.—Completed plication of entire jejunum and ileum. One can readily see how this dependent mass may cause duodenal ileus by traction on the superior mesenteric vessels.

In asthenic patients the completely plicated jejunum and ileum may produce duodenal ileus because of the added pressure on the superior mesenteric vessels. This complication presented a real problem in four of our patients (Figs. 4 and 5.) This observation has caused us to use a complementary duodenojejunostomy in two cases, in one of which the duodenojejunal junction was mobilized and the bowel sectioned and reanastomosed anterior to the superior mesenteric vessels. In all cases in recent years we have passed a Miller-Abbott tube or preferably a small polyethylene tube into the proximal jejunum prior to operation. Fluid and nutritional balance can be readily restored in any case in which postoperative duodenal ileus is encountered.

In the early postoperative period nutritional balance has been readily restored in most cases by early feeding with a slow, constant drip of liquefied whole food, delivered by means of a small food pump. As a result of this forced feeding many of the patients have gone home in a better nutritional state than on admission to the hospital.

Fig. 4.—Note duodenal dilatation. Barium passed through duodenum only when patient was lying down. Relieved by sectioning of proximal jejunum and reanastomosis anterior to superior mesenteric vessels.

Fig. 5.—Severe duodenal ileus with great dilatation of stomach. Relieved by passage of small polyethylene tube into jejunum.

This plication procedure as outlined has been in use for over five years on the surgical services of the Henry Ford Hospital. A total of 40 such operations have been performed. In 17 patients, varying in age from 8 to 60 years, a complete plication of the entire jejunum and ileum has been carried out as a planned procedure. None of the 17 patients had fewer than 3 previous abdominal operations, and one had undergone 22 abdominal sections. Of the 17 patients 7 were taking varying amounts of narcotics for pain relief prior to operation. Duodenal ileus was present in four patients, all of whom were asthenic. Not one of these patients has had subsequent attacks of intestinal obstruction during a follow-up period of from six months to more than five years. Most of the patients have shown a satisfactory weight gain, and none are taking narcotics.

SUMMARY AND CONCLUSIONS

1. The Noble plication operation for controlling peritoneal adhesions in chronic recurring intestinal obstruction has definite value.

2. The operation should be carried out as a planned procedure after careful preparation of the patient, with special emphasis on the nutritional deficiency.

3. The best results are obtained when the entire jejunum and ileum are plicated. Failures result from limited application of the technique.

4. The dependent completely plicated jejunum and ileum may produce duodenal ileus. The prevention and treatment of this complication is discussed.

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Effect of Hydrocortisone in the Prevention of Intraperitoneal Adhesions

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The effects of cortisone and corticotropin (ACTH) on healing tissues have been studied both clinically and experimentally.* In short-term experiments, diminution in formation of granulation tissue and fibrin, inhibition of fibroblast proliferation and leucocyte invasion, reduction in metachromasia, and irregular formation of intracellular matrix are among the observed effects on the connective tissue of skin and bone.† Longer-term experiments have yielded less clear-cut results and suggest that the above sequelae occur only in the early stages of tissue reaction to injury.‡ Nevertheless, the above observations with cortisone and corticotropin have prompted others to study the effects of cortisone and corticotropin on experimentally produced intraperitoneal adhesions.

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* References 1 to 4.

† References 5 to 9.

‡ References 10 and 11.

Thomas, Greene, and Rhoads [5] produced adhesions in rabbits by crushing the cecum with a Doyen clamp. A dose of 12.5 mg. of cortisone was given intramuscularly twice daily for three days before the bowel was crushed and for three days thereafter. In their series, two-thirds of the treated animals demonstrated fewer adhesions than the control animals. Scheinberg and Saltzstein [12] used talc to produce adhesions intraperitoneally in dogs and rats. Either 10 mg. of cortisone twice daily or 5 mg. of corticotropin twice daily was used in the dog; 2 mg. of cortisone daily was used in the rat. A significant reduction in adhesions resulted. Odell, Key, and Taylor,[13] experimenting with rats, demonstrated that intraperitoneal adhesions resulting from a talc suspension could be prevented when cortisone (3 mg. daily in 200 gm. rats) was given intramuscularly either five to seven days prior to the instillation of talc or concurrently with the talc. Magarey and Gough [10] stimulated the formation of adhesions in the rabbit and rat by instilling quartz intraperitoneally. When 20 mg. of cortisone was administered daily to the rabbit and 5 mg. to the rat, they noted an inhibition of fibrosis up to 30 days of treatment. The effect then ceased, and fibrosis ensued. Hubay, Weckesser, and Holden [14] stripped the serosa from a segment of jejunum in dogs. When treated with cortisone (30 mg/kg.) immediately postoperatively, the animals exhibited no reduction in the amount of adhesions. However, when cortisone (30 mg/kg.) was given both preoperatively and postoperatively, an inhibitory effect was manifested. Beamer, Friedman, and Chu [15] treated talc adhesions in mice with cortisone and observed a

temporary retardation of fibrous reaction that persisted for only 12 to 14 days.

Experimental evidence has indicated that hydrocortisone may be the principal hormone secreted by the adrenal gland.[16] It is the principal corticoid hormone found in adrenal gland perfusates,[17] adrenal venous blood,§ and peripheral blood.[20] Therefore, it has been postulated that the observed extra-adrenal effects of cortisone may, in large part, result from a conversion product, viz., hydrocortisone.‖

Our interest in the local use of hydrocortisone was first stimulated by Howard, Pratt, and Bunnell,[23] who used this substance in operative and nonoperative conditions of the hand. They noted a reduced tissue reaction and less stiffness of the hand postoperatively. The efficacy of hydrocortisone locally in certain diseases of the skin, eye, and joints is now well recognized.¶ Therefore, this investigation was undertaken to evaluate the effect of locally administered hydrocortisone acetate on experimentally formed intraperitoneal adhesions.

METHOD

Series I.—Laparotomy was carried out on 9 control and 10 treated mongrel dogs (9 to 10 kg.) under intravenous pentobarbital (Nembutal) anesthesia (30 mg/kg.) and strict aseptic conditions. Thirty centimeters of serosa was stripped with mosquito forceps from the antimesenteric border of the jejunum. Measurement of the length was taken before the serosa was stripped. The width of the area, after stripping, varied from 1.5 to 2.5 cm.

Two weeks later, at the first relaparotomy, the adhesions were photographed and lysed by sharp and blunt dissection. The resulting raw surface area was measured. A polyvinyl catheter (0.064 in. diameter) was then fixed with one 0000 nonabsorbable (silk) suture to the area of bowel involved, brought out through a stab-wound in the flank, and fixed subcutaneously.

Before the abdomen was closed, 50 mg. (1 cc.) hydrocortisone acetate # was applied topically to the raw surface of bowel in the treated animals. Fifty mg. (1 cc.) hydrocortisone acetate was instilled daily through the catheter for two days postoperatively. In the control animals nothing was applied or instilled. The catheter was withdrawn from both the treated and untreated dogs on the second postoperative day.

Two weeks later, a second relaparotomy was done through a fresh wound, and any adhesions were photographed and divided. The resultant raw surface area was measured. A polyvinyl catheter was again fixed to the bowel in the area involved, and identical steps in treatment were carried out as previously. A second set of observations was obtained two weeks later at a third relaparotomy.

Series II.—Five control and five treated mongrel dogs (10 to 15 kg.) were used. The procedure followed was identical to that in Series I, except as follows: 1. Hydrocortisone acetate, 100 mg. (2 cc.), was applied topically at the time of adhesion lysis. Postoperative dosage was the same as in Series I. 2. Control dogs were given a vehicle both topically and through the catheter. The vehicle consisted of the suspending medium without hydrocortisone acetate. 3. Only one series of observations was made.

Series III.—Six control and six treated mongrel dogs (10 to 15 kg.) were used. Anesthetic procedure and aseptic conditions as described in Series I were followed. Five to six centimeters of proximal jejunum was resected, and a two-layer end-to-end anastamosis was performed. A through-and-through running 00 chromic (gut) absorbable suture was used for the inner layer. The serosa was approximated with interrupted Lembert 0000 (silk) sutures. A polyvinyl catheter as used in Series I and II was fixed to the bowel at the site of anastomosis. A dosage schedule similar to that in Series I was employed. The vehicle was given to the control animals. The interval prior to laparotomy and examination of the adhesions was 17 to 21 days.

RESULTS

Table 1 summarizes the results in the treated and the control dogs of Series I. Two weeks after lysis of adhesions and the first course of treatment, two of the control animals had 50% or more reduction in adhesions, whereas five of the treated animals showed similar results. After surgical lysis and a second course of treatment, two of the control and eight of the treated animals had 50% or more reduction in adhesions. The averages for the nine control animals indicate no change in adhesions with each

§ References 18 and 19.

‖ References 21 and 22.

¶ References 24 to 28.

The hydrocortisone acetate used in this experiment was Aqueous Suspension Cortef Acetate, which was supplied by The Upjohn Company, Kalamazoo, Mich.

TABLE 1.—*Results in Treated and Control Dogs in Series I*

Controls: No Treatment: Polyvinyl Catheters in Situ for 48 Hr. Postoperatively							Treated: 50 Mg. (1 Cc.) Hydrocortisone Acetate (Cortef) at Time of Lysis; 50 Mg. (1 Cc.) q. d. × 2 Postoperatively						
Dog	Sex	Serosa Area Stripped, Sq. Cm.	Area of Adhesions Lysed, Sq. Cm.	No Therapy	Area of Adhesions Lysed, Sq. Cm.	No Therapy	Area of Adhesions Lysed, Sq. Cm.	Dog	Sex	Serosa Area Stripped, Sq. Cm.	Area of Adhesions Lysed, Sq. Cm.	Therapy	Area of Adhesions Lysed, Sq. Cm.	Therapy	Area of Adhesions Lysed, Sq. Cm.
0	M	45.0	37.5	..	23.6	..	13.0	00	M	45.0	51.0	..	17.5	..	27.0
2	F	48.0	75.3	..	69.2	..	53.2	1	F	60.0	59.6	..	31.2	..	1.2
5	M	60.0	99.0	..	124.1	..	129.2	3	M	54.0	34.2	..	0	..	0
6	F	60.0	64.0	..	94.7	..	112.0	4	F	45.0	11.2	..	32.3	..	16.1
11	M	54.0	73.0	..	98.0	..	99.5	7	M	54.0	59.5	..	44.0	..	2.0
12	M	45.0	37.0	..	18.0	..	8.0	9	M	54.0	43.6	..	35.6	..	15.0
14	F	57.0	72.4	..	57.7	..	89.6	13	M	60.0	75.0	..	33.5	..	39.9
17	F	60.0	72.0	..	31.0	..	71.5	15	F	69.0	67.7	..	28.5	..	10.8
19	M	45.0	53.0	..	67.3	..	21.4	16	M	60.0	59.2	..	2.0	..	2.0
								18	M	75.0	61.1	..	54.0	..	12.2
		←2 wk.→		←2 wk.→	←——2 wk.——→					←2 wk.→		←2 wk.→	←——2 wk.——→		
		Av.	64.8		64.8		65.4			Av.	55.2		27.8		12.7
		Per cent	100		100		100.9			Per cent	100		50.4		23

TABLE 2.—*Results in Five Control and Five Treated Dogs of Series II*

Controls: 2 Cc. Vehicle at Time of Lysis; 1 Cc. q. d. × 2 Postoperatively					Treated: 100 Mg. (2 Cc.) Hydrocortisone Acetate (Cortef) at Time of Lysis; 50 Mg. (1 Cc.) q. d. × 2 Postoperatively				
Dog	Sex	Serosa Area Stripped, Sq. Cm.	Area of Adhesions Prior to Placebo, Sq. Cm.	Area of Adhesions After Placebo, Sq. Cm.	Dog	Sex	Serosa Area Stripped, Sq. Cm.	Area of Adhesions Prior to Hydrocortisone, Sq. Cm.	Area of Adhesions After Hydrocortisone, Sq. Cm.
92	F	45	64.8	61.2	91	M	45	97.2	24.7
94	F	54	56.5	87.3	93	M	45	72.0	1.0
96	F	45	96.3	154.7	97	M	39	68.0	0.2
98	M	45	67.5	120.0	99	M	39	58.9	25.5
100	F	45	63.1	91.7	101	M	18	86.3	40.5
		←2 wk.→	←——2 wk.——→				←2 wk.→	←——2 wk.——→	
		Av.	63.6	103.2			Av.	76.5	18.4
		Per cent	100	162			Per cent	100	24

TABLE 3.—*End-to-End Bowel Anastamosis (Jejunum)*

Controls: 1 Cc. Vehicle at Site of Anastamosis; 1 Cc. q. d. × 2 Postoperatively				Treated: 50 Mg. (1 Cc.) Hydrocortisone Acetate at Site of Anastamosis; 50 Mg. (1 Cc.) q. d. × 2 Postoperatively			
Dog	Sex	Adhesions Preop., Sq. Cm.	Adhesions After Treatment, Sq. Cm.	Dog	Sex	Adhesions Preop., Sq. Cm.	Adhesions After Treatment, Sq. Cm.
3	M	0	27.8	0	M	0	12.1
68	M	0	24.0	1	F	0	4.0
18	M	0	7.2	15	F	0	5.0
32	M	0	20.5	79	M	0	1.8
52	F	1.5	131.5	67	F	1	5.0
66	M	0	90.9	69	F	0.2	3.5
		←17-21 days→				←17-21 days→	
		Average 50.3 sq. cm.				Average 5.2 sq. cm.	

successive laparotomy and lysis. In the treated animals the area of adhesions after successive laparotomies was decreased by 50% or more.

Table 2 summarizes results in the five control and five treated animals of Series II. All five of the treated dogs and none of the control dogs had 50% or more reduction in adhesions. Among the controls, the amount of adhesion either remained the same or increased. The average area of adhesion in the controls actually increased by 62% after lysis. There was a decrease of 76% in the average area of adhesions in the treated animals.

Table 3 summarizes the results of six control and six treated animals in Series III. The amount of adhesions in the control dogs was generally several times that in the treated dogs. The average for the area of adhesions in the control dogs was 10 times that of the treated dogs. Only one control dog (Dog 18) had adhesions comparable in extent to those of the treated group.

In all three series, maintenance and removal of the intraperitoneal catheter posed no undue problems; no intraperitoneal infections occurred. No difficulties were encountered with any of the anastomoses.

COMMENT

In Series I, the reduction in quantity of intraperitoneal adhesions in the hydrocortisone-treated animals was greater after a second course of treatment following surgical lysis. No adequate reason for this is provided by this study. The dosage of hydrocortisone may have been inadequate. Studies of cortisone and corticotropin effect on wound healing suggest a more marked inhibition of secondary wound repair, where the amount of granulation tissue is greater.[4] Possibly, in Series I, a second lysis initiated a greater reactivity of those connective tissue elements more liable to hydrocortisone action.

In Series II a larger dose of hydrocortisone was used initially; this may explain the more marked results observed. In Series III, however, a dosage schedule similar to that in Series I was used. Yet a more impressive difference in the quantity of adhesions in the control and treated dogs of Series III ensued. In Series III hydrocortisone was applied after initial injury to the serosai, not after lysis of previously formed adhesions. This may have some bearing on the difference in effects observed.

It is possible that the vehicle used in the control dogs of Series II and III may have irritated the tissues and actually abetted adhesion formation. If so, the results of hydrocortisone therapy are all the more impressive, since they were achieved in the face of normal tissue reaction plus the irritative effects of the vehicle.

In addition to a reduction in quantity of adhesions, 75% of the hydrocortisone-treated dogs demonstrated a difference in quality of adhesions. A more filamentous, more easily separable, less fibrotic type of adhesions was formed.

The process of adhesion formation simulates the reaction of most wounds to injury. The injured tissue cells liberate "leukotaxine" and "exudin," which increase capillary permeability and thereby permit the ingress of numerous cellular elements to the involved area.* Polymorphonuclear cells, lymphocytes, monocytes, or wandering undifibroblasts soon appear. A serous exudate containing fibrinogen is discharged. The fibrinogen coagulates, and a sticky fibrous protein, fibrin, is formed. Surrounding tissues become adherent to one another. As the fibrin organizes, cell growth and vessel proliferation ensue. The fibroblasts, which rapidly increase in number, may arise from lymphocytes, monocytes, or wandering undifferentiated mesenchymal cells.[31] The ground substance that is evolved may be secreted by either the fibroblasts or mast cells.[32]

Where in the course of these events do hydrocortisone and the other adrenal cortex steroids intervene? The effects as observed in this experiment can at best only arouse speculation. By inference some suppositions may be advanced, since investigations into the site and mode of action of corticotropin

* References 29 and 30.

and cortisone on healing tissues have yielded a few clues.

Cortisone has been shown to decrease capillary permeability and thereby reduce the inflammatory reaction and mobilization of cells.† An effect on the ground substance and fibroblast formation has also been demonstrated.‡ Ragan suggests that the effect may be upon the cell preceding the fibroblast in development.[31] Asboe-Hansen postulates that the effect of corticotropin and cortisone on the ground substance may be mediated through the mast cells.[39]

Tissue culture studies have yielded contradictory results. Sacerdote,[40] Heilman,[41] and Cornman [42] have shown that cortisone and desoxycortisone inhibit the growth of fibroblasts to varying degrees. These studies indicate a multiplicity of sites where the cortical steroids may operate to inhibit the repair process. Nevertheless, contradictory results by others and variables in the methods and materials used leave uncertain any conclusions as to the site or sites of action of the steroids.[43]

The mode of action of hydrocortisone, cortisone, and corticotropin is unknown; the answer to this problem awaits new tools, techniques, and further knowledge of histochemistry. It is a field of investigation replete with stirring and challenging possibilities.

CONCLUSION

Hydrocortisone acetate applied topically and instilled through a polyvinyl catheter two days postoperatively reduces the quantity and alters the quality of intraperitoneal adhesions that form after experimentally produced adhesions and after resection and anastomosis of a portion of the dog's jejunum.

Mrs. Jane Saxton assisted in the preparation of this paper.

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DISCUSSION

On Papers by Drs. Barron and Fallis, and De Santis, Schatten, and Weckesser

Dr. Elden C. Weckesser, Cleveland: It was with great interest that I listened to the paper by Dr. Fallis and Dr. Barron. We too have had experience with Noble plication, and some of you may remember that three years ago in Toronto, at the meeting of this organization, we presented 10 cases that we had done at that time.

I might briefly give you the follow-up on them. I was able to follow up all but one. The majority of them are doing quite satisfactorily. Two, however, are having intermittent attacks of distress in the abdomen, apparently due to mild intermittent partial obstruction of the small bowel, although we have not reoperated on any of our cases and no definite objective evidence of intestinal obstruction has been observed.

We haven't seen any dilated loops of bowel, such as Dr. Fallis showed. We haven't had any objective signs of obstruction, but two people are having intermittent attacks of distress.

One patient died of intercurrent disease, and apparently was fine as far as his bowels were concerned, although no autopsy was obtained. That leaves us with 6 persons out of the original 10, and they have been living for four and one-half years and are well. The series is small, but I thought you might be interested in that follow-up.

Our feeling at the present time is that the Noble plication operation has a very definite place in our armamentarium, and we tend to reserve it for the very severe case, the case with very extensive adhesions of the small intestine.

We feel very definitely that the technical aspects of the procedure are of importance. I was very intrigued by and interested in Dr. Fallis's procedure of putting the sutures in the mesentery rather than in the bowel wall. In our cases (in my case, at any rate) we have adhered to the procedure of putting them in at the mesenteric margin of the bowel, but it is very important that we allow as much mobility of the intestine as possible. Perhaps Dr. Fallis has a good point in keeping the stitches down in the mesentery to allow more freedom.

It certainly is very important not to sew the bowel tightly at the 180 degree turns at each end of the plication. Leave that as free as possible. We have been very careful about that.

I am not able to follow Dr. Fallis completely in the complete plications. I never have been able to feel justified in so doing, but my mind is open on it. We have reserved the treatment for the badly involved areas of the bowel only.

The work with hydrocortisone has been very encouraging to us. At the present time, in the less severely adherent cases, we have used reperitonealization and 1 to 2 cc. of hydrocortisone acetate locally and hope that our experience will bear us out as being right in that method.

Dr. Fraser N. Gurd, Montreal, Canada: In view of the late hour I shall content myself with citing one human experiment with intramuscular cortisone in the prevention of adhesions.

This young patient served as her own control in this way: In the fall of 1952, a small and rather pretty 19-year-old girl was admitted to the wards at the Western Division, The Montreal General Hospital, for elective appendectomy. Postoperatively obstruction occurred, and after two weeks of conservative management exploration was performed again. A large number of rather vicious adhesions were found involving terminal ileum for a distance of 3 to 4 ft. from the ileocaecal valve. These were all divided, and the patient was placed on intramuscular cortisone. The dosage was 150 mg. daily in divided doses for seven days, which was felt to be a fairly full dose for a 100 lb. girl. After seven days it was cut to 100 mg. per day for three days and then gradually tapered to the end of the second week.

During this two-week interval while on cortisone the patient continued to have obstruction. At the end of the period, after four weeks of almost constant intubation, her condition was poor and frank mechanical obstruction was evident. A laparotomy was undertaken for the third time in a month. Thus, the patient had undergone an exploratory operation two weeks after the appendectomy; adhesions had been observed; she had been put on cortisone, and re-exploration was done two weeks later again.

I can vouch for the fact that at the third operation, despite two weeks of cortisone therapy in the interval since the second operation, the adhesions were much more extensive than they had been, and their quality and toughness were entirely up to standard for that interval. Sharp dissection was required to complete the small bowel lysis, leaving 6 to 8 ft. of small bowel largely denuded of peritoneum. A Noble plication of about 50% of the small bowel was done.

Happily, the patient then recovered and has been completely symptom-free and well for two and one-half years. She has the best end-result of four major plications which I have done. The plication procedure was perhaps life-saving in this instance. It was certainly curative. The parenteral cortisone therapy appeared to be of no value.

Dr. Alfred L. De Sanctis, Cleveland: Dr. Gurd's comments on using cortisone have been

fairly well borne out in much experimental work, and, although the results have been variable, at least in dogs and rabbits, cortisone has been found relatively ineffective in preventing intraperitoneal adhesions.

We use hydrocortisone because of its purported effect on fibroplasia when used locally. By applying it locally, we were able to get a much better concentration of the steroid where we desired its action, whereas either cortisone or hydrocortisone given parenterally will be distributed throughout the body and not act preferentially and maximally at one site.

I made no mention at all about using hydrocortisone in patients. Although Dr. Weckesser has tried it, we have not recommended its use in this paper.

The academic point in all of this, and to me the most stimulating point of it all, is that, for the first time in 60 to 70 years of trying to treat intraperitoneal adhesions, we are using tools that reach the more fundamental levels of tissue.

A review of the literature will show that investigators have empirically tried to put everything from salt to voodoo charms into patients to prevent intraperitoneal adhesions. Nothing ever worked. Now we know of something that will effect tissue healing. Just how it works, we don't know—whether it affects the enzyme systems or whether it attaches to a protein molecule, whether it affects the pH or just what it does—but at least our attention is now directed down to the more basic healing mechanisms.

This whole problem may not end in the hands of the surgeon but eventually in the hands of the biochemist and histochemist, who, working at the level of cell activity, will know what goes on and will be able to prevent wound adhesions.

Collateral Circulation in the Sigmoid Colon

JOHN R. McGOWAN, M.D., University City, Mo.

The blood supply to the sigmoid colon and upper rectum is traditionally related to a "critical point" beyond which ligation will cause necrosis. Most surgeons doubt this theory, but experimental proof is lacking. The arteries to the sigmoid colon and rectum have been reinvestigated with special reference to this question in fresh human autopsy material.

HISTORICAL REVIEW

Sudeck,[1] in 1907, established a "critical point" in the superior hemorrhoidal artery after observing gangrene of the upper rectum in two patients whose superior hemorrhoidal arteries had been ligated just distal to the last sigmoid branch of the inferior mesenteric artery during perineal resection of the rectum. He later found by injection experiments that the vessels of the rectum became filled with injecting material from the inferior mesenteric artery only by traversing a marginal artery above the origin of the last sigmoid branch. If the ligature was placed below the origin of the last sigmoid branch, he found few if any of the rectal vessels filled by injection. Sudeck therefore established the origin of the last sigmoid artery as a "critical point" for maintaining the blood supply of the rectum when ligating the superior hemorrhoidal artery to obtain mobility of the sigmoid colon.

Hartmann and de Dietrichs,[2] in 1909, corroborated Sudeck's findings. They demonstrated by injection that ligature of the inferior mesenteric artery does not affect the circulation of the rectum, provided it is done between its origin and the last important collateral branch, which arises from 1 cm. to 1.5 cm. below the sacral promontory. They also showed that ligation of the terminal portion of the inferior mesenteric artery below the last collateral branch produced almost complete (or even complete) suppression of the arterial supply of the rectum and of the rectosigmoid junction. Hartmann remarked that in perineal excision of the rectum with transplantation of viable bowel to the perineum the superior hemorrhoidal artery must be ligated high on the common trunk, above the last anastomotic loop. Archibald,[3] in 1908, by animal experiments and postmortem dissections, demonstrated the significance of the marginal artery in relation to the blood supply of the sigmoid and upper rectum. He found two danger zones in the collateral circulation of the human colon. The first is the zone of anastomosis between the lowest sigmoid and the uppermost superior hemorrhoidal branches. Here the anastomosis is poor as compared with the bowel above this point, and in Archibald's experiments the injection rarely penetrated to any extent into the upper rectum if the superior hemorrhoidal artery was tied. This vessel runs a long course from its origin in the inferior mesenteric artery over the promontory and down to about the third sacral vertebra before it bifurcates into its terminal lateral branches. In this long course Archibald found few, if any, branches to anastomose with the last sigmoid branch and demonstrated the poverty of communication by injections. The second is the zone of anastomosis between the superior and middle hemorrhoidal arteries, where anastomosis is uncertain. Rubesch,[4] in 1910, also studying

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this region by the injection method, called attention to the fact that the last sigmoid artery, which he called the sigmoidea ima, may be given off below the bifurcation of the superior hemorrhoidal artery and that the so-called "critical point" is not exactly situated but may be encountered within a range of from 13 to 20 cm. from the anus. Manasse,[5] in 1907, emphasized the feebleness of the border vessel in the lower portion of the sigmoid and stated that the last sigmoid artery does not participate in anastomosis to any great extent.

Drummond,[6] in 1914, studied the inferior mesenteric artery of 20 specimens by injection and roentgenograms. He concluded that the last sigmoid branch of the inferior mesenteric artery not only varies considerably in size but that it has an erratic communication with the sigmoid branch above. In 2 of 20 cases the loop between the last sigmoid artery and the anastomosing branch above it was completely absent. In eight cases a loop was present but was so insignificant that one would certainly think it could not carry on the circulation after ligation of the inferior mesenteric artery. In the other 10 a well-marked loop of some size was present. In the majority of cases one or two branches which ran around the bowel on each side and had a little anastomosis above or below were given off from the superior hemorrhoidal artery below the last sigmoid branch. Pope and Judd,[7] in 1929, confirmed the variation in position and number of vessels in the rectosigmoid region. They stated that the so-called "critical point" is always the point of origin of a rectosigmoid artery and that it is, therefore, the first rectosigmoid artery. The region of the rectosigmoid extends from the so-called "critical point" halfway down the rectum. It is a region peculiar in the type of arteries to the wall of the bowel. There are from one to five of these arteries. They may originate from the superior hemorrhoidal artery above, at, or below its point of division at the third sacral segment.

Steward and Rankin,[8] in 1933, on the basis of an extensive study of 100 injected specimens, described a gap in the vasculature of the bowel between the termination of the marginal artery and the bifurcation of the superior hemorrhoidal branch. This segment was found to be supplied by one to five small arteries which arose from the superior hemorrhoidal and which varied in size and number with other anatomic variations in this region, that is, a high, small, or absent last sigmoidal artery or a low bifurcation of the superior hemorrhoidal artery. Sunderland,[9] in 1942, dissected the vessels to the distal colon in 20 specimens and studied the injected arteries of 5 additional specimens roentgenologically. He found the number of sigmoidal arteries to vary from one to seven; they did not form any definite or constant pattern. He discovered that there was a well-marked anastomosis with a continuous vascular arcade ("marginal artery of Drummond") between all sigmoidal arteries. He remarked, however, that his findings disagreed with those of Drummond, who found the lowest sigmoidal artery and its proximal anastomosis to be insignificant in 40% and absent in another 20% of the cases. The experience of Bacon and Smith[10] was similar. These workers confirmed the recommendation of both Sudeck and Hartmann that it is wise in each patient to observe the arterial pattern of the inferior mesenteric artery and its branches before carrying out ligations. Bacon also indicated, in 1950, that the "critical point" has its greatest significance in segmental resection of the sigmoid with end-to-end anastomosis.

Goligher,[11] in 1949, studied the arrangement of the blood vessels to the rectum and distal colon in 75 necropsy-room bodies and supplemented this by observations on 36 patients at operation. He established the following points: 1. If a resection is to be as radical as a combined abdominoperineal excision, it is essential that the ligature on the inferior mesenteric artery be placed not lower than the level of the bifurcation of the abdominal aorta. 2. With the main ligature so sited, it is possible in practically every case to prepare a sufficiently long stump of

sigmoid colon with an adequate blood supply to permit end-to-end union with the rectal stump after resection. This piece of colon is nourished by the first sigmoid artery alone or in combination with the intersigmoid marginal artery or by the descending branch of the left colic artery. Muir,[12] in 1948, stated that, since it is necessary to ligate the inferior mesenteric artery either above or immediately below the last sigmoid branch during a sphincter-saving resection of cancer of the rectum, the blood supply to the distal sigmoid may be jeopardized and it may become necessary to perform an abdominoperineal resection.

Ault, Castro, and Smith,[13] in 1950, reviewed 235 cases of cancer of the rectum and the rectosigmoid and recommended that the relationship of Sudeck's "critical point" to current methods of rectal resection be minimized or even ignored. Their clinical experience demonstrated the functional capabilities of the marginal artery following ligation of the inferior mesenteric artery both distal and proximal to the left colic and first sigmoid branch. These same authors wrote, in 1952,[14] that their clinical observations impressed them with the fact that ligation of the inferior mesenteric artery "at," "on," or "near" the promontory of the sacrum, or "where the vessel crosses the left common iliac," is the usual low level of ligation practiced by many surgeons. Many such ligations have been done because of an erroneous belief in the possible necrosis of the rectal stump and the false application of Sudeck's "critical point" to rectal resections. These workers reported 12 cases of inferior mesenteric ligation cephalad to the left colic branch and illustrated that this ligation is a feasible procedure. They believe that the functional capabilities of the marginal artery are greater than most investigators will acknowledge.

It is quite evident that considerable work has been performed and many observations made relating to the circulation to the sigmoid colon and rectum. It is also apparent that there is no general agreement as to details of the rectosigmoid circulation, particularly with respect to collateral anastomotic channels. The present study was undertaken in the hope of shedding light on this matter.

METHODS

Thirty-three fresh human autopsy specimens were utilized for this study. The results reported herewith were achieved by injection techniques with observation of the specimens in situ during the injecting period and careful further study of the specimens after fixation and clearing by a modification of the Spalteholz technique as described by Noer [15] in 1943.

Injections were carried out as follows (Fig. 1): During the abdominal portion of the autopsy, the inferior mesenteric artery and vein were picked up after minimal dissection and double ligatures were applied to each vessel just below the last sigmoid branch and tributary respectively. After this, complete division of the vessels was carried out between ligatures to insure complete interruption. Glass cannulae were inserted into the aortic origin of the inferior mesenteric artery and near the venous termination of the inferior mesenteric vein. The vascular bed was flushed with human plasma to remove all remaining blood. When the venous outflow became clear, red and blue natural latex solutions were injected into the arterial and venous cannulae. All injections were made under constantly regulated pressures at the level of the patient's antemortem systolic blood pressure. After filling of the vessels, the cadaver was propped up slightly and the pelvic and lower peritoneal cavities flooded with 5% acetic acid solution to "set" the latex.

After the latex solutions became hardened, the entire mass of descending colon, sigmoid, and rectum was dissected off the posterior parietal wall, including the mesentery of the sigmoid and all vessels over to the aorta. The lumen of the fresh intestine was flushed gently with copious quantities of tap water to wash away residual fecal material. The specimen was ligated at each end and then securely tacked onto cork boards. The bowel was inflated with air, just enough to gain a normal intestinal contour but not so much as to cause interference with the vascular bed. The entire preparation was then immersed in 10% formalin for two or three days and then removed and washed under the tap for 24 hours. After washing, the specimens were placed in alternate changes of dioxane until completely dehydrated; then they were placed into methyl salicylate for clearing. After such preparation, the intestinal wall, though transparent, remains visible in its relationship to the arteries and veins. To better record the course

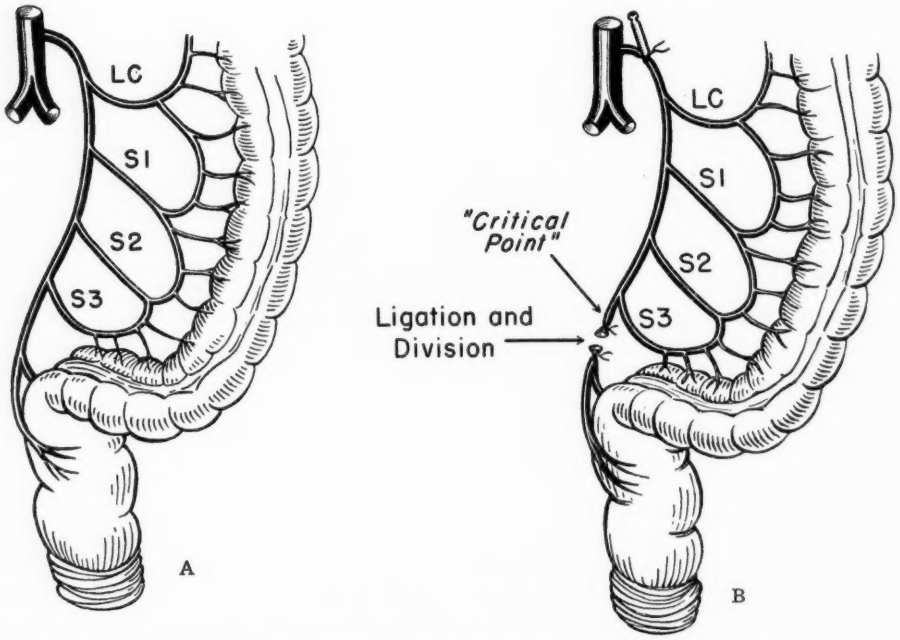

Fig. 1.—*A*, diagrammatic representation of the arteries to the sigmoid colon. Arising from the inferior mesenteric artery are *LC*, left colic; *S1*, *S2*, *S3*, first second, and third sigmoid branches. *B*, experimental procedure: ligation below the "critical point" before injection via the cannula at the aortic origin of the inferior mesenteric artery.

of collateral filling in situ and to check the results obtained, color cine photography of the actual vascular filling was carried out during injection with red latex solution and with India ink diluted with human plasma.

RESULTS

Of the 33 fresh human colon specimens studied, all showed adequate collateral circulation to the sigmoid and rectum after ligation and division at the "critical point." This was evident both immediately after the injection process, while the specimen was in situ, and also after the specimens were fixed and cleared. In every one of the 33 specimens studied, the superior hemorrhoidal artery and all its branches were filled with injection media, despite ligation and division at the "critical point" (Fig. 2).

All the specimens were carefully inspected for the presence of an anastomotic arcade between the last sigmoid branch and the superior hemorrhoidal artery. This did not exist in any of the 33 specimens; yet in all of them the rectal vessels were well filled with the injecting medium.

COMMENT

Accepted means for studying circulation include dissection, injection, and experimental ligature in living animals. The latter method is limited, particularly in studying the human colon, because of lack of strictly comparable vascular patterns in the usual laboratory animals. Dissection techniques, while valuable in the case of larger vessels, are tedious and apt to be misleading with respect to finer vascular channels. Injection techniques, particularly in fresh human cadaver material, have many advantages.

Certain limitations must be placed upon the interpretation of findings achieved by this method. Steward and Rankin, after extensive experience with this type of work, pointed

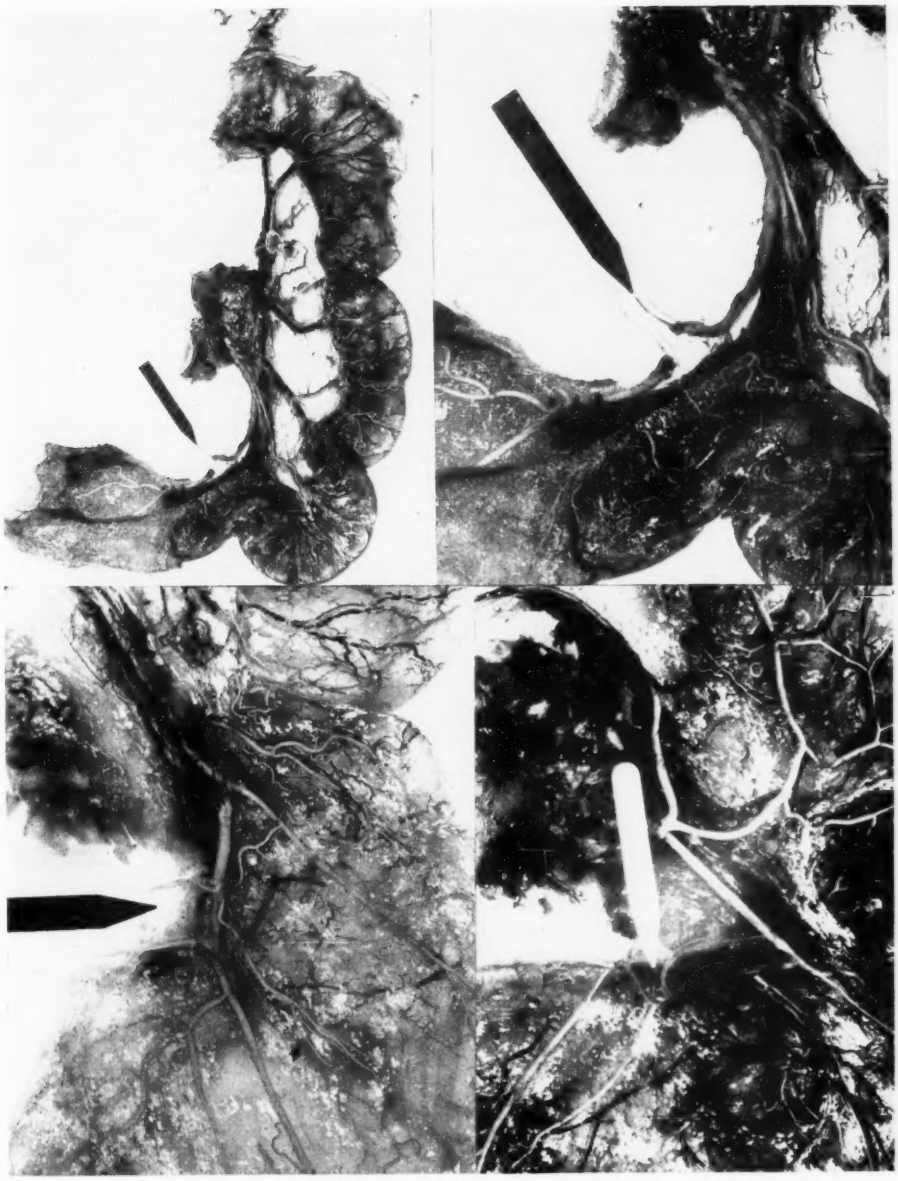

Fig. 2.—The two upper illustrations are of the same specimen. The illustration to the right is a close-up of the area of ligation. In both, note the excellent filling of the rectum and rectosigmoid (to the left of the arrows) despite ligation at the "critical point."

out that, as a means of studying the course, relationship, and anastomosis of vessels and of preserving a permanent record of the specimen, injection techniques are satisfactory. They indicate, however, a feeling that it may be impossible as well as dangerous to draw conclusions from such work regarding the vascular potentialities of these same vessels during life.

On the other hand, there is experimental justification [16] for guarded use of injection studies in evaluating collateral circulatory routes. It has been shown that maximum intestinal devascularization compatible with life in experimental animals is comparable to the maximum which will still permit complete injection; circulatory interruption of a degree which will cause intestinal necrosis in animals may be predicted by incomplete filling with injection media. Thus, while such studies of collateral circulation are not necessarily conclusive so far as living conditions are concerned, they are still probably the best available means for studying anastomotic channels. They must be accepted as of considerable value in estimating situations as they exist in living man.

CONCLUSIONS

1. No arterial arcades were found between the last sigmoid and superior hemorrhoidal arteries in any of the 33 specimens studied.

2. Injections revealed good collateral circulatory channels to the sigmoid and rectum after ligation and division of the inferior mesenteric artery below the last sigmoid branch.

3. Intramural anastomotic channels appear to be the means whereby rectosigmoid circulation is maintained following ligation of the inferior mesenteric artery below the last sigmoid branch.

4. These studies indicate that the "critical point" of Sudeck is of little or no importance in the maintenance of rectosigmoid circulation.

DISCUSSION

DR. CHARLES G. JOHNSTON, Detroit: I want to express my appreciation for having been able to look at this paper before this meeting. There are two points I should like to discuss. The first is in relation to the paper.

It is quite obvious that injection techniques in the dead body cannot give us all the information that we might get if it were possible to do the same thing on a living person, because of the differences in tone of the vessel, the possibility of thromboses in the living person, and one additional situation which Dr. Noer has so aptly shown. In the living animal with injected specimens of the small bowel, he was able to show that distention regularly destroyed the mural anastomosis. Dr. McGowan has shown fairly well that there are good anastomotic channels through the intestine, even though the area is not well supplied with large vessels.

I have always been very much concerned about the critical angle. There is little question that, anatomically at least, it is a very poorly vascularized area and an area which should be treated with respect. Nevertheless, all of us at times have left a little shorter cuff on the rectal side and found no difficulty with it. It is, however, an area that should not be tampered with, even though it seems that one can take more liberties with it than one would expect by anatomical considerations.

The other point I want to bring out is one that has always been of interest to me, primarily because it was a great personal feeling of pride with me that when I was a medical student my teachers were willing to allow me to do a few things that I believe were worth while trying to find out a little more about, which were not necessarily in the books, and they took the viewpoint that if you really want to know a procedure you had better try it. I think that viewpoint in relation to medical students who have an interest in determining something is very, very important.

There are two schools of thought among medical faculties. One is that students should be taught; they should be given their instruction by their teachers; they should listen and accept what is given to them as gospel, because there is so much to learn that if they try to do a little thinking on the side they might not learn some important point.

All of us know that a good many of the things we teach today are not so tomorrow, and it is because of young men who have some interest in delving into such things that we change our viewpoints. So, I believe it is well worth while, when a student has an interest in doing a bit of research, that faculties give him every opportunity to exercise this bit of personalized imagination.

DR. D. W. MCLEAN, Detroit: I should like to say a word about the clinical application of the findings which Dr. McGowan has so beautifully demonstrated.

Clinically, there is another factor in this problem. At operation when the bowel is transected, the col-

lateral circulation in the bowel wall, on which we depend for the circulation in the rectosigmoid, is interrupted. Therefore, when the inferior mesenteric or superior hemorrhoidal artery has been ligated and the sigmoid and its mesentery resected, leaving the rectosigmoid or upper rectum in place, the circulation in this distal segment must depend entirely upon the inferior hemorrhoidal artery.

The question is, is it safe to depend upon that circulation in all cases? We have seen gangrene of the rectosigmoid and upper rectum in two cases where such an operation was carried out. Both of these patients were over 70 years of age. We have done this operation repeatedly in patients under 60, with no trouble. Therefore, we have concluded that in patients with advanced arteriosclerosis or in patients over the age of 70 it is hazardous to depend upon the circulation from the inferior hemorrhoidal artery to take care of the rectosigmoid.

In those cases where the rectosigmoid and upper rectum were removed and the anastomosis made between the upper sigmoid or descending colon and the lower half of the rectum, we have had no trouble. We have never seen gangrene of the upper segment following ligation of the superior hemorrhoidal or inferior mesenteric arteries.

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Recurrent Carcinoma of the Rectum and Rectosigmoid

Results of Treatment After Continence-Preserving Procedures

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and
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Carcinoma of the rectum and rectosigmoid may recur locally regardless of the type of surgical procedure employed.* It has long been realized that the treatment of local recurrences after combined abdominoperineal resection is largely futile.[1] Total excision of the malignant tissue is practically never possible, and external irradiation is of limited value even palliatively. Relatively little is known of the results of treatment of local recurrences after continence-preserving procedures, such as segmental resections and pull-through operations. On the whole, the results should be better than those of treatment of recurrences after combined abdominoperineal resections. The presence of the bowel should permit earlier recognition of the recurrence, since the region in which the recurrences develop is accessible to both digital and proctoscopic examination. The recurrence may involve only the wall of the bowel or the perirectal tissues which can be resected. Radiation therapy should be more successful also, since radium and possible interstitial irradiation may be employed in addition to roentgen therapy.

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Section of Surgery, Mayo Clinic and Mayo Foundation, (Dr. Black), and Fellow in Surgery, Mayo Foundation, (Dr. Kelly). The Mayo Foundation, Rochester, Minnesota, is a part of the Graduate School of the University of Minnesota.

* References 1 and 5.

However, in fact, local recurrences after continence-preserving procedures are usually not recognized until they are far advanced. While the recurrence may be limited to the bowel in an occasional case, some degree of fixation to the wall of the pelvis has usually occurred by the time the diagnosis is made. Neighboring structures are involved frequently, and the scarring and fixation resulting from the first surgical procedure make all subsequent attempts at resection most difficult. In addition, as with all locally recurring carcinomas, distant metastases, precluding any possibility of cure, are often present.

The present study was undertaken in an effort to evaluate the results of treatment of such recurrent lesions. All cases at the Mayo Clinic from 1940 through 1949 in which the lesion had recurred locally after a continence-preserving procedure were reviewed. In many cases, the original lesion had been treated elsewhere, and information regarding the kind and extent of the primary lesion in these cases was largely lacking. However, in all cases, the primary lesion had been, in all probability, within reach of the 24-cm. proctoscope. A segmental resection (low anterior resection) had been carried out in the majority of cases. In others a pull-through procedure had been employed, while in a few cases the original lesion had been exteriorized, and the temporary stoma subsequently closed. No effort was made to compare results after surgical procedures of the different types. A serious effort was made to exclude secondary primary lesions from consideration, since the results after treatment of lesions of this type are materially better than those after recurrent lesions.

In all, 116 patients who had recurrent lesions were seen during the decade. The recurrent malignant tissue extended into the lumen of the bowel in 109 cases, while in the remaining 7 it was palpable through the wall of the bowel or within the perineum. The recurrence was proved by biopsy in all except nine cases. Eight of the nine patients are known to have died and the ninth is presumably dead. In four cases only was the local recurrence above the level of the true pelvis. Of the 109 cases in which the recurrence extended into the lumen of the bowel, the location of the recurrence with respect to the anastomosis was known in 75. Of these, the recurrence had developed clearly at the site of the anastomosis in 55, below the level of the anastomosis in 12, and within the perineum or at the level of the levatores in 8.

A discussion of the genesis of local recurrence after colonic resections, and, particularly, after resections at the level under consideration, is largely beyond the scope of the present paper. The great proportion of cases in which the recurrence developed at the site of the anastomosis is in keeping with the findings of Cole [2] and with those of Goligher, Dukes, and Bussey.[4] Lofgren,[6] in an independent pathologic study of most of the cases in the present series, concluded that the recurrences could be best explained in fully 75% of cases on the basis of implantation of viable malignant cells within the anastomosis. His finding that recurrences at the site of the anastomosis were no more frequent in cases in which lymph nodes were involved than in those without nodal involvement suggests strongly that unresected involved nodes are not responsible for the recurrence. Presumably, in the usual case, free malignant cells in the lumen of the bowel become implanted in the cut ends of the bowel or are carried into the wall of the bowel during the process of suturing. McGrew, Laws, and Cole [7] found that 82% of smears taken within 5 cm. of the lesion were positive for malignant cells and that smears taken from as far as 35 cm. from the lesion were occasionally positive. Vink's [8] experiments using rabbits suggest that implantation occurs far more readily if the bowel is previously prepared with antibiotics, as is routinely done at present in colonic surgical procedures.

It should be pointed out, however, that recurrences of other origins are possible, since local recurrences are commonly seen after combined abdominoperineal resection, frequently when the lumen of the bowel has not been entered. Recurrences resulting from unresected lateral extensions, from unresected involved nodes, or from exfoliated cells outside of the lumen of the bowel cannot be prevented by irrigation of the bowel, as suggested by Goligher and his colleagues [4] or by the isolation of the lesions by ligatures as suggested by Cole.[2] Such measures, however, should unquestionably be used routinely.

TABLE 1.—*Type of Treatment of Recurrent Carcinoma After Continence-Preserving Procedures*

Treatment	Patients	
	No.	%
None*	12	10.3
Irradiation	70	60.4
Lesion treated locally	4	3.4
Abdominal exploration	30	25.9
Lesion not resected	13	11.3
Palliative resection	5	4.3
Nonpalliative resection	12	10.3
Total	116	100.0

* Recurrent lesion not treated; colonic stoma established in seven cases.

TREATMENT

The treatment of patients in the present series varied from none to radical resection. In general, if total removal of the recurrence seemed possible, and if there were no known distant metastases, resection was advised, contingent, of course, on the general condition of the patient.[3] Otherwise, irradiation was employed unless the recurrence was so extensive or the patient's condition so poor that any type of treatment seemed contraindicated (Table 1).

No Definitive Treatment.—The recurrent lesion was not treated in 12 of the 116 cases. In 7 of the 12 a palliative colonic stoma was established because of bowel obstruction. The formation of a stoma was not thought advisable in anticipation of possible obstruction,

and, indeed, in all cases the procedure was carried out with reluctance.

Radiation Therapy. — Seventy patients were treated by means of irradiation. Usually the lesion was so fixed and extensive that resection seemed out of the question. In other cases, distant metastases were known to be present, and in some the condition of the patient precluded surgical treatment. A colonic stoma was established in 20 of the 70 cases, not only to relieve obstruction but, in some cases, to facilitate the use of radium or radon. The fecal stream was also occasionally shunted from the site of the recurrence in the hope that the fixation would lessen, in time, sufficiently to permit resection. Radium, applied proctoscopically directly to the lesion, was used in the majority of cases; others, in addition, received external roentgen treatment, while a few received only treatment of the latter type.

TABLE 2.—*Survival After Irradiation for Recurrent Carcinoma After Continence-Preserving Procedures*

Interval After Treatment, Yr.	Deaths Within Interval	Survived to Beginning of Interval	
		No.	%
0-1	42	70	100.0
1-2	15	28	40.0
2-3	6	13	18.6
3-4	1	7	10.0
4-5	1	6	8.6
5+	1	5	7.1
6 or more	4	4	5.7

Considering the radioresistance of rectal and colonic carcinoma in general and the limited response to irradiation of recurrences after combined abdominoperineal resection, the results were surprisingly good (Table 2). While 42 patients (60%) died within one year of treatment, 7 patients lived three or more years and 5 lived for at least five years. Three patients were living at the time when this paper was written, 10, 11, and 14 years, respectively, after treatment, and one other patient died of a cerebrovascular accident 8½ years after the appearance of the recurrence. There was no evidence of rerecurrence at the time of death.

Local Treatment of Recurrent Lesion.— The recurrent lesions of four patients were treated locally. In two, polypoid recurrences at the suture line were treated by fulguration. One patient died four and one-half years later of generalized carcinomatosis, and one was apparently well at the time of writing, five years after treatment. Radical resection was apparently thought inadvisable in both cases because of the general condition of the patients. The third patient had a single nodule of recurrent carcinoma in the posterior vaginal wall. The nodule was excised locally and the patient has remained well since, an interval of approximately five years. In the last case, a nodular recurrence developed in the perineum just behind the anus. The patient died 56 months after the local excision of recurrent localized and generalized carcinomatosis.

Attempted Radical Reresection. — After clinical examination, an attempt at radical reresection was considered advisable in only 30 of the 116 cases. In 4 of the 30 cases hepatic metastases were found and no effort was made to resect the recurrent lesion. The lesions proved to be so fixed at operation in nine other cases that resection could not be carried out. In five cases palliative resections were carried out. In probably none of the five were palliative resections originally considered. In each, the dissection had progressed to a point at which the procedure could not be terminated short of resection before it was clearly evident that not all of the recurrent tissue could be resected. One of the five patients died postoperatively. The late results after the palliative reresections were most unimpressive. All four patients who survived the procedure died as a result of the carcinoma within 18 months.

All known gross carcinoma was resected in the remaining 12 cases. One patient died postoperatively. The late results were reasonably satisfactory. Two of the 11 patients who survived the postoperative period were living without evidence of recurrence, seven and eight and one-half years after treatment, while another patient lived slightly more than five years before dying of carcinomatosis. Of

the remaining eight patients, one died within one year, five within three years and two within four years after treatment.

The surgical procedures employed and the difficulties encountered in the 17 reresections are of some interest. Combined abdominoperineal resection in one or two stages was carried out in seven cases. Resection of the involved segment of colon with primary reanastomosis was carried out in seven cases, while in three an exteriorization procedure was done. The dense scarring resulting from the first surgical procedure made mobilization of the bowel difficult in all cases and most difficult in those cases in which the rectum had been mobilized from the hollow of the sacrum at the time of the first operation. The bowel was often broken into during the course of the dissection. While serious bleeding from rupture of great vessels was not encountered, the possibility of breaking into the left iliac vessels particularly was a constant hazard. Ureters were resected or transplanted in two cases; segments of the small bowel were resected because of malignant invasion in two cases, and involved portions of the abdominal wall were removed in three cases. The uterus, ovaries, or posterior vaginal wall was resected in several cases.

No planned pelvic exenterations were carried out. Indeed, no case in the group seemed particularly suitable for a procedure of this type. Either the recurrence was limited to the bowel or perirectal tissues and could be adequately removed or it had become fixed to the sacrum or lateral pelvic walls and could not be resected. The latter was the usual cause of local inoperability.

COMMENT

The findings in the present study clearly indicate the gravity of local recurrences after continence-preserving procedures. Prevention is obviously far more important than treatment, and measures to prevent implantation of malignant cells at the site of the anastomosis, as previously mentioned, should be taken routinely. The findings definitely indicate also that local recurrences are treatable and that the outlook is not necessarily hopeless. It could well be pointed out that the surgical practices of the 1940's are not necessarily those of the present. Unquestionably, in a greater proportion of cases exploration is being performed at present than during the decade covered in the review.

If the majority of local recurrences do result from implantation of malignant cells at the site of the anastomosis, which seems most probable, the recurrence should involve only the region of the anastomosis. Furthermore, for a time at least, the involvement should remain limited to the bowel or pericolonic or perirectal tissues. At this stage, in theory, reresection should be possible. At a later stage, local fixation precludes any possibility of reresection; hence operability depends on the degree of fixation, excluding from consideration distant metastases and the condition of the patient.

In all but the most superficial recurrences limited to the wall of the bowel, the degree of fixation is most difficult to judge clinically. After low segmental resections, the bowel is always more or less fixed by scarring and, in cases in which the rectum has been mobilized from the hollow of the sacrum at the original procedure, there may be dense masses of scar tissue posteriorly. Since some degree of fixation is expected in all cases, exploration should probably be advised unless the recurrent lesion is completely fixed to the pelvic wall or sacrum.

Even after the abdomen has been opened, local operability may not be determinable until after a rather extensive dissection. Resection should not be attempted unless there is some certainty that the recurrent lesion can be resected totally. Judging from the present series, the results after palliative reresections are much inferior to those after irradiation. As previously discussed, one of the five patients failed to survive the surgical procedure and none of the four who recovered lived longer than 18 months.

If the recurrent lesion is found inoperable, irradiation should be advised, not only for purposes of palliation but with possibility of prolonged arrest or even of cure. Probably the most unexpected finding in the present

study was the fact that 4 (5.7%) of the 70 patients treated by irradiation were apparently cured. This rate is a poor estimate of the effectiveness of irradiation, since many patients so treated had hopelessly extensive local recurrences or distant metastases. This is borne out by the fact that 42 of the 70 patients died within one year of treatment and 15 more within the second year. A far longer duration of life would be expected among patients whose only recurrence involved the anastomosis. If patients dying within two years of treatment are excluded, the results after irradiation were quite comparable to those after resection.

SUMMARY

One hundred sixteen cases of recurrent carcinoma of the rectum or rectosigmoid after continence-preserving surgical procedures were seen at the Mayo Clinic from 1940 through 1949. The lesions in 104 cases were treated. Four of seventy patients treated by irradiation, two of four treated by local excision or fulguration, and two of eleven who survived radical reresection were living without evidence of further recurrence five or more years after treatment.

The results indicate that treatment of recurrent lesions of this type is not necessarily hopeless. In spite of formidable technical difficulties, radical reresection should be attempted if distant metastases are absent and if the local lesion can be resected totally. The results after palliative resections are so poor that palliative resection should not be attempted. The results after irradiation were unexpectedly good and were not limited to palliation in that 4 of the 13 patients who survived for more than two years were apparently cured.

DISCUSSION

DR. CHARLES D. BRANCH, Peoria, Ill.: My personal experience with this type of recurrence is limited. With the increase in the use of the anterior resection I feel sure that this problem will be more frequently seen. As Dr. Warren Cole is unable to be here today, he has given me permission to quote his statistics. In the first 50 cases reported by Dr. Cole, there was a 10% recurrence rate, all of these recurrences at the site of anastomosis. This series has now reached 150 cases, and the recurrence rate is staying approximately the same—9.6%, and all at the suture line.

The prevention of such a complication is prophylaxis at the time of the original surgery. As Dr. Cole has suggested, one possibility is that of ligating the bowel above and below the lesion before any manipulation is performed.

Secondly, preliminary venous ligation should be carried out in the most proximal portion of the regional mesentery to prevent tumor spread. Dr. Rupert B. Turnbull, of Cleveland, has shown the need of this so well. In his experiments he was able to recover tumor cells from the major mesenteric veins in 32% of the cases of colorectal carcinoma examined.

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The Significance of the Dumping Syndrome

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and
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The postgastrectomy, or dumping, syndrome is a common and severe complication following total gastrectomy and occurs not infrequently after partial gastrectomy.* Since there has been confusion as to the mechanism of this syndrome, it was decided to study a series of cases. It was our feeling that if the true mechanism could be clearly established proper therapy might then be instituted. For the past two and one-half years a group consisting of members of the surgical physiology unit, the gastric service, and the biochemistry service of the Memorial Center has been studying this problem. Because of the interest by the gastric service in total gastrectomy as the treatment for cancer of the stomach and with this material at hand, the major emphasis of this study has been on this type of patient.

The syndrome consists of a feeling of fullness, churning, or discomfort in the epigastrium, occurring shortly after eating a meal or taking a hypertonic solution. This is then followed by nausea, weakness, sweating, pallor, tachycardia, lasting from 60 to 90 minutes, followed by gradual improvement and a feeling of well-being until the next meal. During the acute episode the patients almost invariably wish to lie down. In severe cases vomiting and diarrhea may play a prominent part. The major response in this syndrome is sympathetic in nature, but how this response occurs has not been clearly shown. Many theories have been advanced to explain it. It has been thought that the response was due to an actual distention of the jejunum due to rapid dumping of food or solutions into it, causing a stimulation of the splanchnic nerves, with a sympathetic outflow responsible for the varied manifestations of the syndrome. Balloon distention of the jejunum has been carried out by investigators to show that this mechanism is involved.† However, it has been shown that distention of the jejunum does not consistently produce the typical symptoms,[5] nor does blocking of the splanchnic nerves, either by resection or by pharmacological blocking agents, abolish it.‡

Smith [6] has shown that there is a drop in plasma potassium and phosphate with electrocardiographic changes which are characteristic of hypokalemia during the dumping syndrome and implicates this as the mechanism. Pontes [7] has postulated that hyperactivity of the adrenal cortex plays an important role in the syndrome because of retention of sodium and chloride and a drop in eosinophiles during the phenomenon. Hypoglycemia following hyperglycemia [8] and hyperglycemia alone [9] have been implicated.

METHODS

Because of the confusion as to the mechanism, it was decided to utilize in the study all methods that might help to clarify the syndrome. Chemical, mechanical, and metabolic studies were done. These consisted of serial electrocardiograms, determinations of plasma volumes, hematocrit values, and blood pressure measurements, and potassium, chlo-

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* References 1 and 2.

† References 3 and 4.

‡ References 1 and 5.

ride, glucose, phosphate, and bicarbonate determinations. On four gastrectomized patients, renal function studies, electrolyte excretion measurements, and eosinophile counts were calculated. On three patients balloon distention studies of the jejunum were done. Basic studies were carried out on six patients with intact stomachs, acting as controls; on four patients with total gastrectomies and esophageal-jejunal anastomoses; on three with total gastrectomies and esophageal-duodenal anastomoses; on four with Ross-Robertson procedures (substernal esophagojejunostomy); on four with total gastrectomies and ileocecal transplants (esophago-ileo-colo-duodenostomy); on one with total gastrectomy and jejunal transplant (esophago-jejuno-duodenostomy); on one with jejunostomy (stomach intact), and on four with partial gastrectomies with gastrojejunal anastomoses. These were carried out at frequent intervals after the introduction of various solutions: (1) 9% sodium chloride, (2) 50% glucose or fructose, (3) Sustagen,§ and (4) starch. It was necessary to quantitate the solution given to each patient, in an attempt to avoid diarrhea. The amount of hypertonic solutions usually ranged between 100 and 200 cc. In certain cases serial electrocardiograms were taken before and after a routine hospital meal, and no measurements of plasma volume were done on these cases because of the interfering lipemia following ingestion of food.‖ The technical details of these studies have been previously described.[10]

The results of these studies are consistent and of interest.

RESULTS

Alterations in Blood Volume.—1. Hypertonic Solutions: There was a marked decrease in plasma volume occurring within 10 minutes after introduction of the solution, reaching its maximum in approximately 30 to 40 minutes, and returning to normal in 100 to 120 minutes (Fig. 1).

2. Foodstuffs: Surprisingly enough, with a high carbohydrate meal or a starch solution which was actually hypotonic to the plasma at the time of ingestion, there was a marked decrease in blood volume similar to that observed with hypertonic solutions. This was studied in six patients, and it was found that rapid hydrolysis of the starch solutions took place with a breakdown into many smaller molecules, accounting for the increased osmolarity and the resultant decrease in plasma volume. This is well illustrated by a comparison of the blood volume level following hypertonic glucose and a hypotonic starch meal.

In summary of the total-gastrectomy patients, all showed decrease in plasma volume following hypertonic solution, Sustagen, or starch. One patient with total gastrectomy had to be given more than twice the usual amount in order to produce the dump. Two of four patients with partial gastrectomy failed to dump on the usual hypertonic-

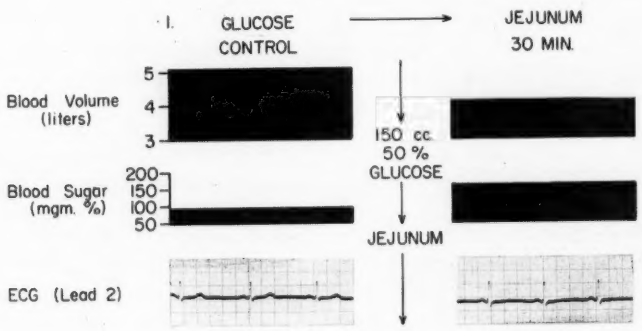

Fig. 1.—Relationship between the changes in blood volume, blood sugar, and electrocardiogram before ingestion of 150 cc. of 50% glucose in totally gastrectomized patient and 30 minutes later, at the height of the dumping syndrome.

§ Carbohydrates 66.5%; protein 23.5%; minerals 4.0%; fat 3.5%. The Sustagen used was donated by Mead Johnson & Company, Evansville, Ind.

‖ Recently plasma volume determinations have been done, using I^{131}, on these patients.

solution routine. None of the controls showed alteration in plasma volume (Fig. 2).

Electrocardiographic Alterations.—Within 10 to 15 minutes following the administration of hypertonic solutions, Sustagen, starch, or, in certain cases, routine hospital meals, the electrocardiogram showed characteristic alterations in all patients exhibiting the dump. There was a flattening of the T-wave, elevation (or occasional depression) of the ST segments, and the occasional appearance of a U-wave. These changes were maximal in 30 to 40 minutes and returned to normal in 80 to 120 minutes. Lead II, as a rule, showed the changes better than the other leads. Again, one patient with total gastrectomy and two with partial gastrectomies failed to dump on the usual routine and also showed no electrocardiographic alterations. None of the six controls with stomach intact showed electrocardiographic changes (Figs. 1 and 2).

Electrolytes.—There was a progressive fall in potassium and phosphate in patients given hypertonic glucose. This included both gastrectomized patients and controls. The fall reached a maximum after 90 minutes and was usually still well below normal after all signs of the dump had disappeared. Also of interest is the fact that when 9% sodium chloride was used, the gastrectomized patient exhibited clinical symptoms and signs of the dump, with change in blood volume and electrocardiographic changes but no alteration in potassium or phosphate, the explanation for this being that when glucose is given the potassium and phosphate are withdrawn from the extracellular fluid and deposited with the glycogen.[11] We believe that the depression of the potassium or of the phosphate has no relation to the dump syndrome.

Renal Excretion.—It was found in four patients measured that renal excretion of sodium and chloride was decreased after hypertonic glucose solutions. This confirms work previously published.[7]

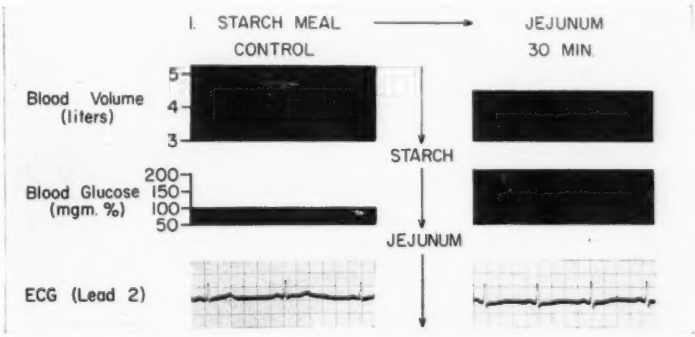

Fig. 2.—Relationship between the changes in blood volume, blood sugar, and electrocardiogram before administration of 150 gm. of starch and 30 minutes later, at the height of the dump syndrome.

Eosinophiles.—In four patients studied there was a drop in the eosinophile count, in one patient at 90 minutes. In the other three there was no change noted during the dumping syndrome.

Jejunal Distention.—With balloon distention with air or water up to 200 cc. there were epigastric discomfort and nausea in all three patients studied. However, there was no change in plasma volume, hematocrit value, or electrocardiogram. Also, rapid administration of water or barium mixture (200 to 800 cc.) in an attempt to cause distention failed to produce any significant change in the blood volume or the electrocardiogram or any symptoms.

COMMENT

It seems clear to us from our studies [10] and those of others ¶ that the dumping syndrome is caused by a rapid shift of circulating fluid from the blood stream into the small intestine. There appear to be several variants in the production of this fluid shift (Fig. 3). With a hypertonic solution, such as 50% glucose or fructose, the fluid shift probably occurs in order to bring the intestinal contents into isotonicity with the plasma. With a hypotonic solution of starch there must be a rapid enzymatic hydrolysis, with the breakdown of a small number of large molecules with low osmotic attraction into a great number of small molecules with a high osmotic attraction. The marked shift in fluid can be accounted for in this manner. This is clearly shown by a comparison of blood sugar levels and plasma volumes in a gastrectomized patient given 50% glucose with those in a patient given a starch meal. They are similar (Figs. 1 and 2).

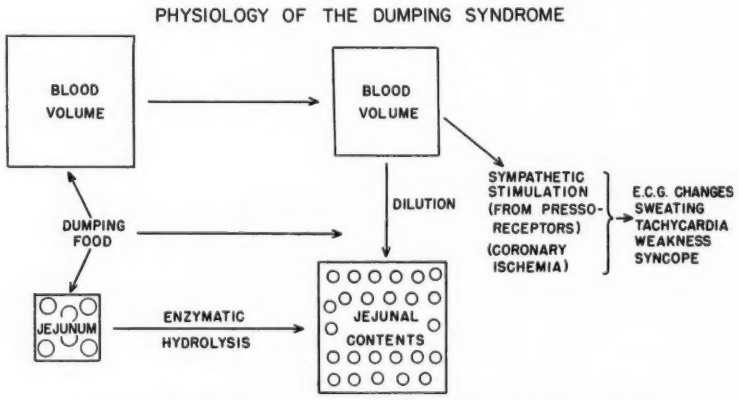

Fig. 3.—Our conception of the mechanism of the dumping syndrome.

With the acute shift of fluid one can easily explain the sympathetic response with all of its symptoms, including the electrocardiographic changes. What we are dealing with is a shock-like state due to rapid loss of extracellular fluid. Within the past month we took one of our dumping patients and repeated her experiment, giving her 100 cc. of 50% fructose on which she had previously dumped. However, this time we infused 500 cc. of a plasma volume expander (Expandex) rapidly at the time of the expected dumping syndrome. The result was that the plasma expander corrected the fluid shift, and, consequently, we had no dump symptoms and no changes in plasma volume or in the electrocardiogram.

After we had clarified the syndrome to our satisfaction, it appeared to us that what we needed was a reservoir in place of the stomach, which would slowly release ingested food into the intestinal tract. Let me add that this idea is not original. However, the ileocolic transplant of Dr. Good, of Denver,# appealed to us. Unfortunately, we found that, although by x-ray after a barium meal the transplanted colon appeared at first to act as a reservoir, actually what happened was that the barium would remain in the transplanted segment only until a wave of peristalsis sent most of it gushing into the duodenum. A severe dump would then occur. We have not been ingenious enough to devise a surgical operation which would insure us that the patient would not dump. In fact, after total gastrectomy, we believe, all patients will dump unless they are

¶ References 4, 12, 13, and 14.

We were given the opportunity to study four of these patients by Drs. Frederick Good and Henry Swan.

careful as to the type and amount of food they take at one time. We have found that after total gastrectomy most patients will not gain weight but, in fact, will lose it. In 15 out of 20 gastrectomies studied in our outpatient department, we found the caloric intake was less than 1500 calories (Table). Why? These patients are literally afraid to eat. They have found by experience that if they increase their caloric intake they will dump.

For the past year, and the work is still in progress, the surgical physiology unit and the biochemistry service have been studying the dietary aspects of the total gastrectomized patient. We have found that by cutting carbohydrates, which are rapidly hydrolyzed, to a minimum and increasing protein and fat the dumping syndrome can be controlled. With the use of frequent feedings (approximately six feedings a day) and the addition of protein and fat supplements, we have been able to increase caloric intake above 2500 calories. With this regimen all patients studied have been able to gain weight, and the dumping syndrome has been satisfactorily reduced in most of them. This is not an ideal type of diet but it is far better than a low-calorie diet which is not sufficient to maintain the nutrition of a person. It should be emphasized that, although carbohydrates are mainly responsible for the production of the dumping syndrome, a patient can and will dump on a high protein meal if too much food is given at one time. A study of the occurrence of the dumping syndrome on various test diets is in process and will be reported at a later date.

Caloric Intake Study on Forty Patients with Subtotal Gastrectomy, Twenty with Total Gastrectomy, and Four with Total Gastrectomy with Ileocecal Transplants.

Intake, Calories	Number of Cases		
	Subtotal Gastrectomy	Total Gastrectomy	Ileocecal Transplants
< 800	8	5	3
<1,200	9	5	0
<1,500	9	5	0
<1,800	4	2	1
<2,000	5	0	0
<2,200	2	1	0
>2,200	3	2	0
Total	40	20	4

CONCLUSIONS

1. The dumping syndrome occurs frequently after total gastrectomy.

2. It is caused by a rapid shift of circulating fluid from the blood stream into the jejunum.

3. A high-protein, low-carbohydrate, diet is of value in controlling it.

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DISCUSSION

ON PAPERS BY DRS. JOHN M. WALKER, KATHLEEN E. ROBERTS, ALBERT MEDWID, AND HENRY T. RANDALL AND CAMPBELL GARDNER AND JAMES R. MCCORRISTON.

DR. H. S. MORTON, Montreal, Canada: I should like to compliment Dr. Walker for his excellent presentation. His remarks regarding the value of a solid diet are borne out by our work on the electrical reactions of the stomach. I thought it might be interesting to remind you of some of the findings that we have had with fluids and solids. Dr. Goodman at the Presbyterian Hospital in New York and we in Montreal have been measuring the electrical changes during the ingestion of milk. The positive or negative response depends on the site of the electrode in the stomach—if it is on the greater curvature, as it is in 85% of cases, the potential difference becomes more negative, whereas if it is on the lesser curvature it goes up or positive. The same change occurs with all other fluids—beer, whisky, tomato juice, orange juice, and water. Solids, on the other hand, give no change whatever in the P. D. after a time interval of anywhere from 20 to 45 minutes, associated with the same symptoms as those of the dumping syndrome.

Concerning Dr. Gardner's paper—at the Royal Victoria Hospital we have done the Hofmeister procedure in well over 1000 cases, and the figures are very similar to those that Dr. Gardner showed. The persistence of complaints is higher in those cases with short duration of symptoms and continuation of the patient's ecology. Dr. Dragstedt referred to the nervous element in the causation of duodenal ulcer. Penfield and Faulk, at the Montreal Neurological Institute, investigated the movements of the stomach during operations on the insula and found that if Area 16 is stimulated there is a marked augmentation of the gastric motility. If the insula is totally ablated there is inhibition of movement. Thus we believe there is cortical control from the insula to the hypothalamus and so on down through the vagus.

DR. LOUIS T. PALUMBO, Des Moines: I find it difficult to stand up here and to make comments after these two electrifying presentations. I would like to compliment Dr. Gardner and Dr. Walker and their associates on their excellent presentation and studies. They open many avenues for us for consideration, but I'm sure time will not permit full coverage of these various phases.

In the series we have studied we found that not all of our patients developed a dumping syndrome: As indicated in a recent survey of 189 partial gastrectomies, 18% of patients developed a dumping syndrome; in 42 in which we combined a bilateral infradiaphragmatic vagus resection, 19% developed a dumping syndrome, and only 5% of our patients with total gastrectomy developed this syndrome.

I think we are producing in these patients a physiological disturbance which is difficult for them to react to, that is, certain percentages of persons. In these operations we certainly are cutting (intentionally or otherwise) the vagal pathways to the gastrointestinal tract and are producing, then, possibly an imbalance in certain persons on the sympathetic side.

As Dr. Walker's group has shown, this definitely is a syndrome as a result of overstimulation of the sympathetics. However, not all patients develop the syndrome, and, therefore, they have the ability, I believe, to adjust to these physiological disturbances that we are producing in these patients when we operate on them. However, a high percentage of our patients do not have this syndrome, and therefore we must assume that they are capable of adjusting to this stress situation without apparent clinical physiologic changes.

Therefore, in some there is an overactivity or stimulation of the sympathetics. As we know, the sympathetics control a variety of functions in the body. One is sudomotor (sweating) activity; another is vascular control; a third is dilatation of the bowel, and a fourth is visceral afferent (pain) pathways. This probably can bring about the responses described by Dr. Walker.

I must agree with Dr. Gardner that it is very difficult to set up an evaluation program in relationship to any gastric surgical procedure. As he has pointed out, there are many things one must establish in one's plan prior to an investigation, so that these things are properly recorded in the patient's chart, so that the person who is doing the evaluation can make it accurate.

In 1947, we believed that by combining a partial gastrectomy with a bilateral infradiaphragmatic vagus resection we might eliminate or diminish the severity of the dumping syndrome by producing gastric retention due to a delay in the emptying time of the gastric remnant. We found on repeated and long follow-ups with barium roentgenographic studies of the stomachs of our patients with only a partial gastrectomy that the gastric remnant normally emptied in 45 minutes, whereas, in the group in whom we combined the partial gastrectomy with a bilateral vagus resection, the emptying time of the gastric remnant was three to four hours. This delay in emptying time in the latter group we believed might eliminate the dumping syndrome, but, as you

see on these slides, the dumping syndrome occurred in about the same degree and severity, and the incidence is about the same in the two groups.

We, also, have produced other physiological changes in these two groups. In 100% of the patients with a bilateral vagus resection and a partial gastrectomy, there is a persistent achlorhydria, whereas in the other group, with only a partial gastrectomy, achlorhydria occurred in 65%. This can produce certain physiological changes in the gastrointestinal tract functions as well as systemic manifestations dealing particularly with red-blood-cell formation.

Another important thing is that we have disturbed the motor activity of the gastrointestinal tract when we perform a bilateral vagus resection, as noted on this slide.

In the group with a partial gastrectomy, 98% of the patients on barium motor meal studies revealed a normal gastrointestinal function both of the stomach and of the small bowel pattern. However, in those patients on whom a vagus resection and a partial gastrectomy were performed, we found that in 40% (and it has persisted now for six or seven years) there was a hypomotility of the small bowel, clumping, puddling, and segmentation; these changes are similar to those found in cases of regional enteritis. Here, again, we are producing marked physiologic changes which may result in gastrointestinal disturbances creating symptoms.

In 21% of our patients with the combined operation we have noted diarrhea; however, in only 8% of the patients with partial gastrectomy alone was this a troublesome complaint. Marginal ulcer did not develop in any of the patients with the combined vagus and gastric resection procedures, whereas there was a low incidence, of 1.3%, in the partial gastrectomy group. Time does not permit me to furnish many other important comparative items in these two groups.

Dr. Claude J. Hunt, Kansas City, Mo.: I would like to confine my remarks to paper No. 27, presented by Dr. Walker.

I was very much interested in what he had to say concerning the dumping syndrome. He discussed the problem of the malnutrition that is associated with total gastrectomy, and it is to that point that I wish to confine my remarks.

I am quite sure that all of you are familiar with the very bad results, from the standpoint of nutrition, and other effects that are associated with the standard operation of total gastrectomy, namely, esophagojejunostomy with enteroenteroanastomosis. These people don't have any food basket. They can't eat very much, and consequently they have these bad end-results.

Efforts have been made by many to substitute some portion of the gastrointestinal tract for the stomach or to make a pouch so these people can eat. Dr. Walker referred to the operation of transplanting the right colon, which has been done by several persons. I have not been very enthusiastic about that procedure.

In the first place, I have never thought the colon could be very well substituted for the stomach. It is anatomically and physiologically unsuitable. Secondly, when you remove the right colon you remove a large reservoir for water absorption. Many patients have frequent stools, as they do after right colectomy for a surgical lesion. This is undesirable. Others have taken the transverse colon and replaced the stomach by a segment of it. This, to me, is objectionable.

Longmeier and Henley have used a segment of the jejunum to replace the stomach, which I believe is the most anatomical and physiological portion of the gastrointestinal tract, if you want to take any part of it to replace the stomach. This gives a good tube and maintains the relationship to the duodenal contents.

If you take two segments of the jejunum and make an enteroenteroanastomosis between them and replace the stomach with that, from the esophagus to the duodenum, you have a large bread basket and the patient can eat. Again, the operation we prefer, which we have done in nine cases with good results, is a Roux-Y type of procedure with the formation of a food pouch out of the distal limb of the jejunum. I believe a Roux-Y should be done in all total gastrectomies to divert the duodenal contents and to prevent reflux esophagitis.

If you divide the jejunum 12 in. or so below the ligament of Treitz and to the Roux-Y and then bring up the distal end of the jejunum and anastomose the esophagus well back from the end of the jejunum, then fold the end down and make a stoma between the distal end and the ascending limb, you then have a large pouch, more comparable to the stomach than the stomach remaining after a subtotal gastrectomy. These patients can eat, they don't lose weight, they don't get anemic, and they don't have distress from reflux esophagitis.

Dr. Robert M. Zollinger, Columbus, Ohio: Both Dr. Walker and Dr. Gardner deserve to be congratulated for their excellent studies. It is very refreshing to have someone admit that the dumping syndrome is a real problem in gastric surgery and occurs rather routinely after total gastrectomy. I gather from Dr. Walker's remarks that there is nothing very satisfactory about any substitute gastric pouch and that we have to come up with something better.

I also was glad to hear both authors mention the fact that this dumping syndrome occurs after any type of gastric operation. It certainly has been our experience that if you talk to these people personally

and accept the fact that any type of gastric complaint can be lumped together under that broad term of "dumping," then we find that 30% to 40% have it early after surgery, regardless of the type of procedure. I suspect that we would have fewer dumping symptoms if we used a smaller stoma, as Dr. Dragstedt has indicated.

We have carried out studies similar to those reported by Dr. Walker. We found the same shifts in plasma volume and we concur in his interpretations of these findings. The shift may be rather marked, and it occurs after almost any type of operation. We have observed it after vagotomy and gastroenterostomy in patients having a severe dumping syndrome.

However, we have had one patient seven and one-half years after total gastrectomy in whom we have had difficulty in producing the dumping syndrome. We have had a somewhat different experience as far as starch is concerned, in that the deficit in plasma volume did not show up until the starch had eventually broken down.

For a number of years we have always recommended, as have most of you, that the gastric case should stay away from sugars, especially at breakfast. Our dietitians have long insisted on giving these patients solid food during the early postoperative period. Twelve ounces in solid food does better than twenty ounces of liquid food. They have custards, toast, and seasoned foods, and invariably we have told whoever cooks for these patients to set aside ¼ lb. of butter in the refrigerator each day, to be used the first thing in the morning on toast; so the patients have to reverse a lifelong tendency to start off with cereal and, instead, use heavy butter and toast, and so on.

Our best results was the man who had had total gastrectomy seven and one-half years ago. He enjoys beer and pretzels while watching television at night, and I might suggest to the previous speakers that they study the effect of alcohol and pretzels on the dumping syndrome. Perhaps they can discover a method of completely overcoming this objectionable sequela of gastric surgery.

Dr. John M. Dorsey, Evanston, Ill.: I had no intention whatever of discussing any of these papers, as good as they are, but I am prompted to ask, how many of us have undergone a gastric resection? I happen to have had one, and I will say this about it:

If the indications which are used to decide upon gastric resections are as carefully followed on your patients as they were on me—and I hope I am using them on my own—then I think we will have very little complaint or concern, either conscience-wise or otherwise, about how we are handling our peptic ulcers.

Most patients who have had gastric surgery, even those who have the dumping syndrome, would not trade back for what they had in the past if the criteria for the surgery are well founded.

Dr. John M. Walker, New York: I would like to conclude by thanking Dr. Zollinger and the other discussors for their interest in this paper.

In summary, we believe that the mechanism of the dumping syndrome is that of a rapid shift of circulating fluid from the blood stream into the intestines; that the syndrome plays an important role in the morbidity of the total gastrectomized patient, and that it is often the cause of malnutrition and failure to gain weight. Patients because of it are afraid to eat. If they eat any sizable quantity of food, especially carbohydrates, they will dump. Any patient whose nutritional status is poor after gastrectomy deserves to be studied. A careful history with the objective tests that we have outlined will implicate the dump if present. A high-protein, high-fat diet with frequent small feedings may be of real value, and on this regimen the patient may show a gain in weight and life may become quite tolerable. As of today we know of no operative procedure that will protect against the "dump" after total gastrectomy.

Dr. Campbell Gardner, Montreal, Canada: I have one thing to say in closing.

I have two living patients with total gastrectomies after eight years, one with lymphosarcoma and one who had an ulcer from whom I took out the entire stomach believing a cancer present. Curiously enough, neither of them has the so-called "dumping" symptoms.

Megaesophagus

Surgical Therapy

DONALD B. EFFLER, M.D.
and
JAMES W. ROGERS, M.D., Cleveland

Megaesophagus is a common disease characterized by dysphagia and abnormal dilatation of the organ. Although recognized for many years and the subject of numerous clinical and physiologic studies, the entity is not understood from the standpoint of etiology. It is indeed fortunate that specific therapy has been provided in a disease whose exact nature is unknown.

The terms cardiospasm, achalasia, and megaesophagus are used interchangeably. This is unfortunate and adds confusion to a subject already obscured by clinical mythology. The terms cardiospasm and achalasia imply lack of relaxation of the so-called cardiac sphincter. In other words, the circular muscle of the terminal esophagus, smooth and involuntary in action, fails to relax in coordination with the act of swallowing, and dysphagia results. This condition is extremely variable in degree and in itself does not constitute an irreversible problem. Every physician is familiar with the cardiospasm manifested by the emotional patient who is unable to eat anything but the most carefully selected diet and yet never demonstrates obvious nutritional deficiency. In such a patient it is rarely possible to demonstrate organic pathology by the most careful radiographic and endoscopic studies. Functional cardiospasm, as this is generally considered to be, usually responds to a wide variety of therapeutic drugs and dilatation procedures. Although the response to such treatment may be gratifying, good results are rarely permanent and are frequently clouded by other manifestations of functional distress. The most important feature of functional cardiospasm is its lack of structural change. In other words, functional cardiospasm, or achalasia, is not followed by progressive dilatation of the esophagus; neither is megaesophagus the end-product of simple mechanical obstruction.

Megaesophagus is an organic disease and is associated with obvious structural change. Whereas there may be considerable variation in degree, the esophagus reflects definite abnormalities in its dynamics and morbid anatomy. The disease occurs at all ages. The youngest in our series (32 patients) was 24 years old and the oldest 74 years. Although many of our patients presented the clinical picture of underlying anxiety tension, correction of the organic defect was rewarded by prompt relief of dysphagia without relapse. Patients with megaesophagus may present severe nutritional disturbances, with profound weight loss and the appearance of frank starvation; this is not so in functional cardiospasm.

Whether megaesophagus is related by its pathologic features to megacolon is difficult to prove; changes in the myenteric plexus and disturbances in the nerve-muscle relationship have been claimed. Certainly the clinical features of megaesophagus and megacolon are analogous, even though the basic pathologic features may not be identical. It is also apparent that the structural change of megaesophagus is not the end-result of simple obstruction alone; long-standing fibrous strictures of the terminal esophagus

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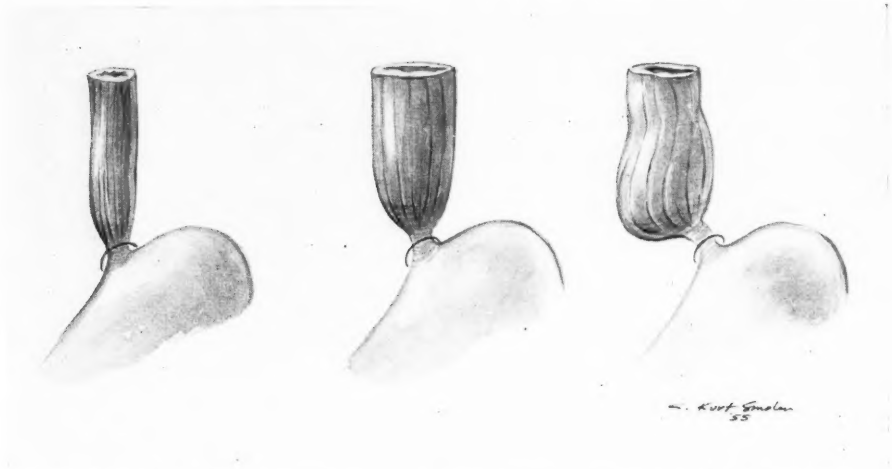
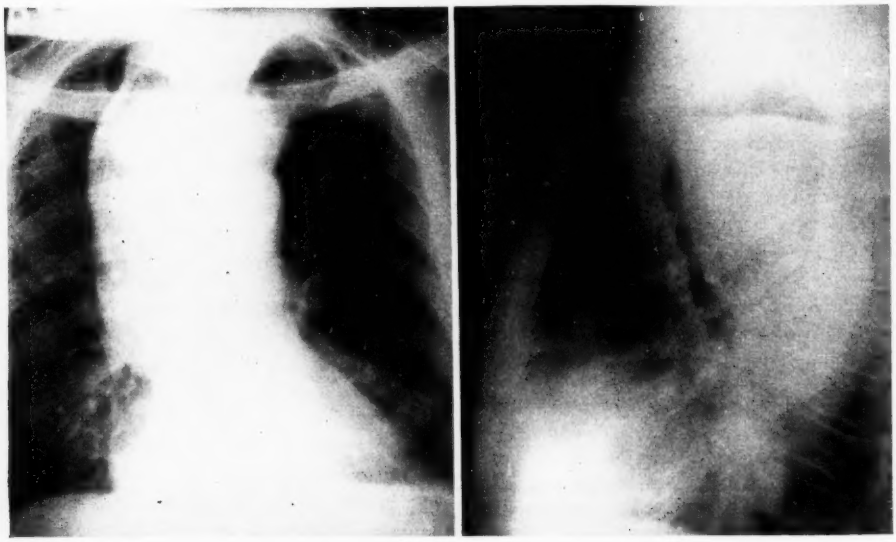


Fig. 1.—Diagrammatic conception of the gross changes characteristic of megaesophagus. The figure on the left represents the normal esophagus and its relation with the esophageal hiatus and stomach. This may be seen in functional cardiospasm but it is not distinguishable from the normal. In megaesophagus the organ may be of normal length or may show some degree of tortuosity. In both cases there is a tendency toward a spindle-like narrowing at the esophagogastric junction.

or occluding neoplasms do not produce the picture of megaesophagus (Fig. 1).

In our opinion, megaesophagus is a distinct disease entity of unknown etiology featured by a pathologic contraction of the circular muscle in the cardiac esophagus and proximal dilatation of the organ. We have not seen evidence of peptic esophagitis, peri-

Fig. 2.—Radiographic appearance of megaesophagus with marked retention within the thoracic esophagus. The fluid level is apparent at the level of the sternal notch. Anterior displacement of the trachea and deviation of the mediastinal structures are apparent on the lateral film.



esophagitis, or abnormalities of the esophageal hiatus. Because of the constant feature of terminal smooth-muscle contraction and associated dilatation, it appears that megaesophagus is a specific disease and not the end-product of long-standing functional organic obstruction. Impairment of the patient's nutritional status is a common feature and is proportional to the severity of the primary disease.

CLINICAL FEATURES

The diagnosis of megaesophagus is based on clinical history and radiography. The usual history includes a period of dysphagia and food retention. It is not unusual for the patient to relate episodes in which he has regurgitated undigested food that may be identified with meals taken a day or two before. Total obstruction may occur when a bolus of meat or fibrous membrane (e. g., skin of a prune or apple) acts as a plug in the narrowed terminal outlet of the esophagus. Characteristically these patients do not have the symptoms of peptic esophagitis or other forms of indigestion. The weight loss is directly proportional to the degree of mechanical obstruction at the cardia and the secondary retention. Pulmonary symptoms are not uncommon in cases where aspiration occurs; in severe cases the bulk of a dilated esophagus, with its large volume of retained food elements, may reduce pulmonary function by compression (Fig. 2). Repeated episodes of aspiration may further reduce pulmonary function by basal pulmonary fibrosis.

Radiographic study will offer a conclusive diagnosis in the majority of cases. With simple cardiospasm the esophagus may be quite normal in appearance, with some delay as the barium enters the stomach. In megaesophagus the organ must clearly show dilatation and impairment or absence of normal peristalsis. As illustrated here (Figs. 3 and 4), the dilated esophagus may be normal in length or greatly exaggerated by development of tortuous folds; in severe cases the esophagus may be half again its normal length, and at the point of greatest dilatation

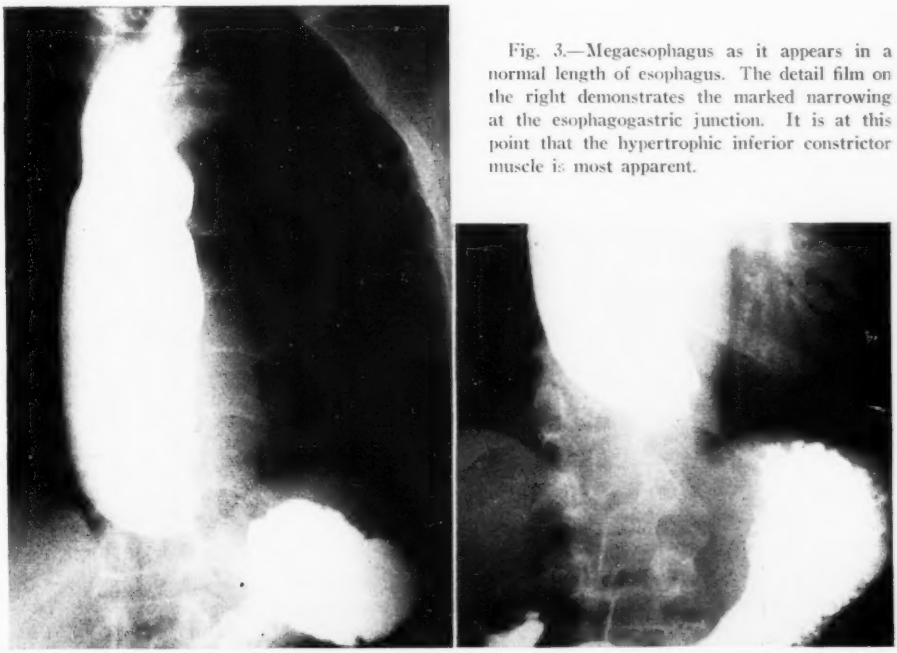


Fig. 3.—Megaesophagus as it appears in a normal length of esophagus. The detail film on the right demonstrates the marked narrowing at the esophagogastric junction. It is at this point that the hypertrophic inferior constrictor muscle is most apparent.

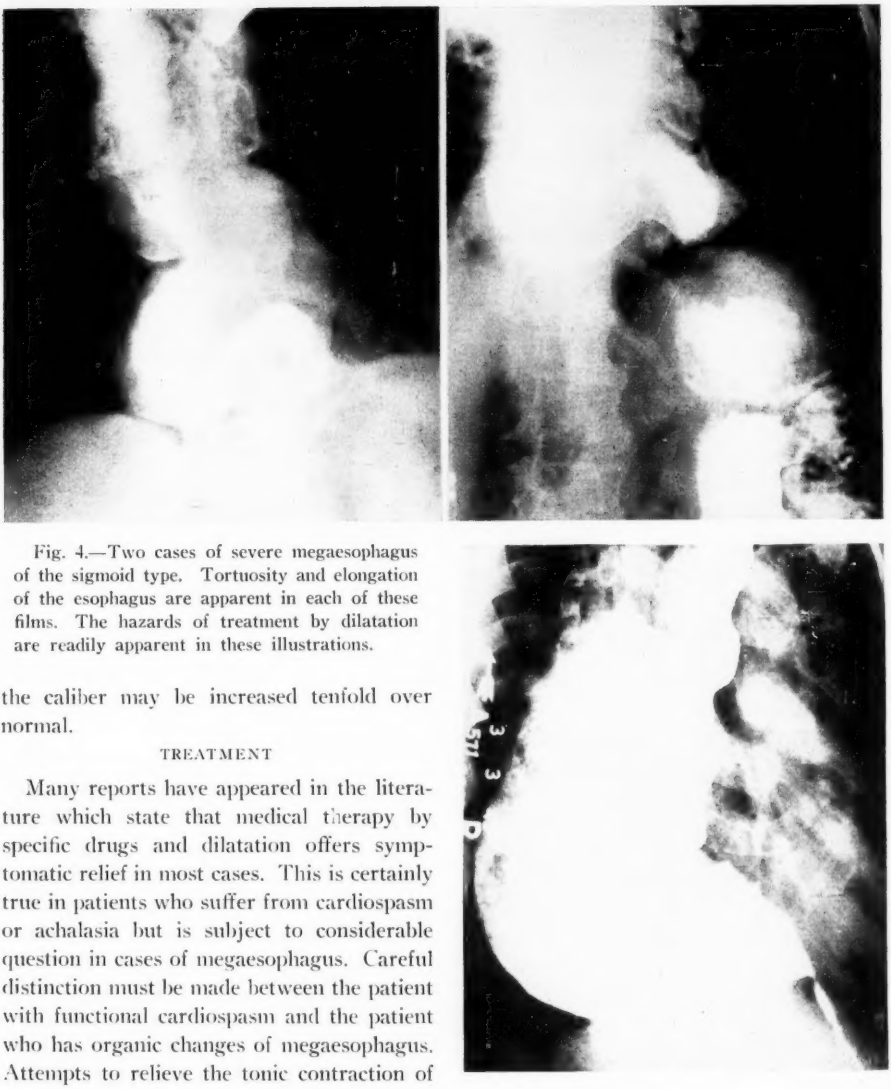


Fig. 4.—Two cases of severe megaesophagus of the sigmoid type. Tortuosity and elongation of the esophagus are apparent in each of these films. The hazards of treatment by dilatation are readily apparent in these illustrations.

the caliber may be increased tenfold over normal.

TREATMENT

Many reports have appeared in the literature which state that medical therapy by specific drugs and dilatation offers symptomatic relief in most cases. This is certainly true in patients who suffer from cardiospasm or achalasia but is subject to considerable question in cases of megaesophagus. Careful distinction must be made between the patient with functional cardiospasm and the patient who has organic changes of megaesophagus. Attempts to relieve the tonic contraction of the cardiac sphincter and megaesophagus by sympathomimetic drugs, sedatives, antispasmodics, or procaine derivatives have been singularly unsuccessful. The surgeon is particularly impressed with the inefficacy of conservative management when his patients describe long periods of oral therapy and their unimpressive results. It seems likely that the esophageal cesspool with its food retention, in megaesophagus would be a poor conductor for any agent, even if it were specific for the underlying problem.

A wide variety of dilatation procedures have been recommended in the treatment of megaesophagus. There may be a place for bouginage in selected cases where the esophagus is not tortuous. However, a fair number of our patients have had repeated dilatations over a prolonged period of time, with transient improvement only and a significant

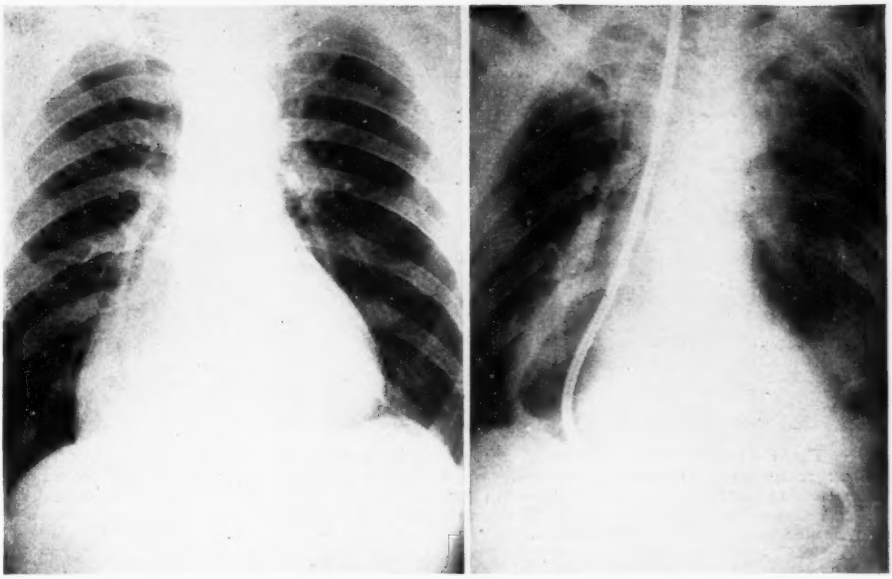


Fig. 5.—Widening of the cardiac silhouette by severe megaesophagus may lead to an erroneous diagnosis of pericardial effusion or heart disease. In the above case the immediate postoperative film (right) clearly differentiates between the cardiac silhouette and the superimposed tortuous esophagus with its retention material.

financial drain. Patients with the sigmoid type of terminal esophagus offer a structural pathway that is not conducive to safe dilatation. The risk of perforation is well known and the hazard of bouginage increases directly with the tortuosity of the organ.

Direct surgical intervention is the treatment of choice. In our opinion it is to be recommended to all patients who have clinical evidence of true megaesophagus and who present no obvious contraindication to surgery. In reviewing the literature, one finds that the surgical intervention for the treatment of megaesophagus has employed both the abdominal and the transthoracic routes. Although many operations are described, they vary primarily in detail and all conform to one of three basic approaches: (1) the esophagogastroplasty, (2) the linear myotomy, and (3) subtotal resection and anastomosis of the esophagogastric cardia. Many of the men famous in modern gastrointestinal surgery have made contributions in principle or detail to the surgical therapy of megaesophagus. The historical features of surgery in megaesophagus have been well recorded and will not be repeated at this time.

ESOPHAGOGASTROPLASTY

Our first efforts in the correction of megaesophagus employed the Heineke-Mikulicz principle of esophagocardioplasty (Fig. 6). This procedure, performed through a transthoracic approach, was designed entirely to increase the size of the esophagogastric lumen and to relieve any element of obstruction in this manner. Considerable care was taken to perform the procedure under direct vision with a careful interrupted nonabsorbable surgical (silk) suture technique and to insure a residual opening between esophagus and stomach that would remain patent despite any cicatricial contraction. This operation was performed in 12 patients and was then discontinued when its obvious sequelae became apparent. In all but three patients the operation was rewarded by relief of the obstructive symptoms but penalized

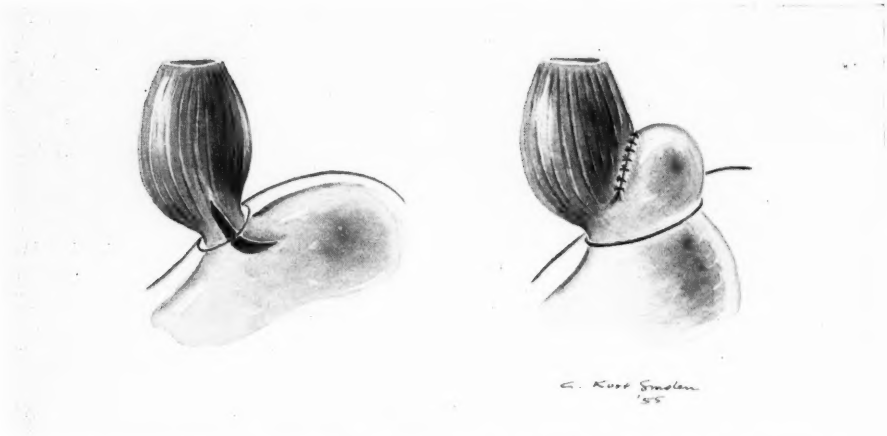
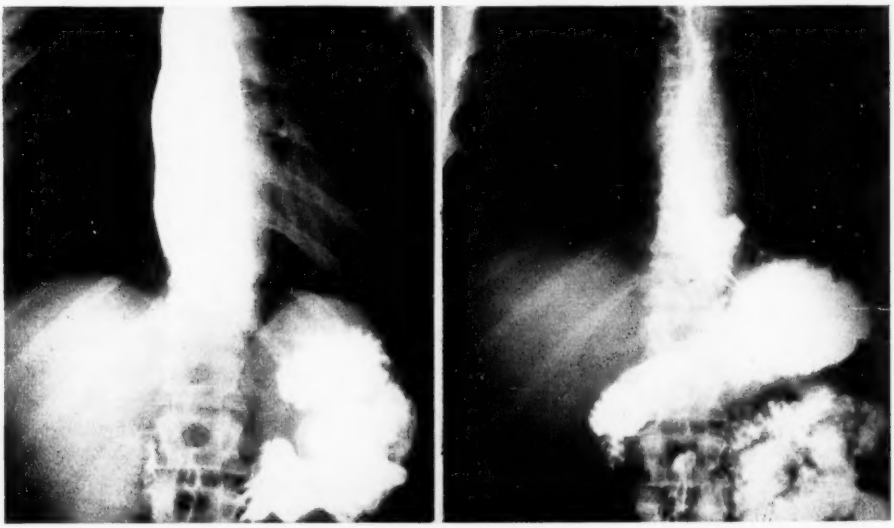


Fig. 6.—Diagrammatic description of the Heineke-Mikulicz principle in the treatment of megaesophagus. The initial incision is carried through all layers of esophagus and cardiac stomach (left). The transverse closure will result in elevation of the stomach through the hiatus to create a surgical artifact similar to that seen in a small hiatus hernia. Gastritis and reflux esophagitis are the expected complications of this procedure.

by a new symptom complex suggesting reflux esophagogastritis. These patients complained bitterly of intolerable heartburn and retrosternal pain that would occur shortly after ingestion of food and was relieved only by large amounts of antacids, upright position, and self-imposed starvation. These symptoms were so severe that it became necessary to reoperate upon eight of these patients. At second operation the terminal esophagus

Fig. 7.—Radiographic studies of a patient with megaesophagus treated by the Heineke-Mikulicz principle. The postoperative film (right) demonstrates marked reduction in the caliber of the organ as the obstructive manifestations are completely relieved. The surgical artifact and secondary ulceration within the small thoracic stomach led to abandonment of this procedure; secondary operation for correction was mandatory in eight cases.



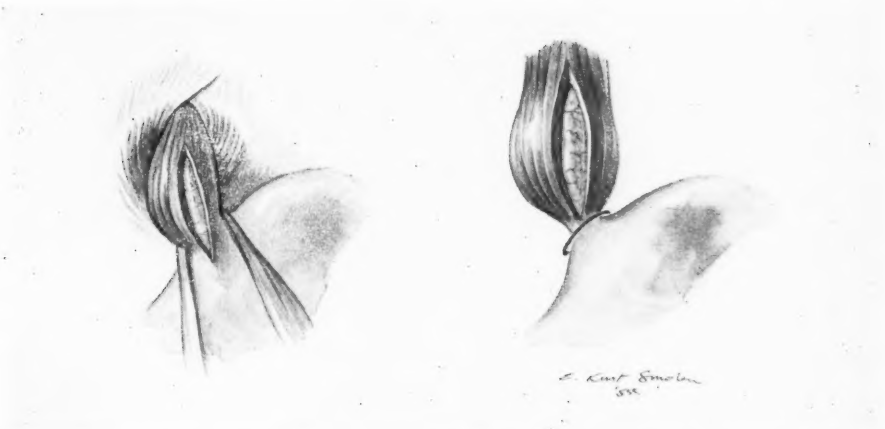


Fig. 8.—Artist's conception of the principle of linear esophagomyotomy. The figure on the left demonstrates the infradiaphragmatic approach; the transthoracic approach is demonstrated on the right.

was again mobilized and the esophagogastric junction reduced below the diaphragm in a manner employed by us in the surgical treatment of a short esophagus. It is interesting to observe that all these patients were promptly relieved of their symptoms of reflux esophagitis, even though the esophagocardioplasty itself was not taken down and was in no way altered. This observation has led to the assumption that esophagocardioplasty, as we employed it, corrected the original dysphagia but superimposed a second disease similar to that of hiatus hernia with short esophagus. This assumption is supported by the second observation that simple transthoracic reduction of this artificial thoracic stomach offered prompt relief of the symptoms produced by the original surgical artifact.

Three patients have received complete relief of their symptoms of dysphagia and retention by this esophagocardioplasty procedure, in spite of the above-described surgical artifact; none have complained at any time of peptic esophagitis or related symptoms. However, all are elderly patients; two were over 70 years of age and the third admitted to 67 years. Although no physiologic studies were performed, it is postulated that achlorhydria and reduced gastric secretions may have been factors that prevented the reflux symptoms which occurred in the younger patients. A period of four years or more has elapsed since operation, and none of the elderly patients have shown late complications or unpleasant sequelae.

LINEAR MYOTOMY

Dissatisfaction with the unpleasant side-effects of the esophagocardioplasty prompted us to employ linear myotomy of the terminal esophagus. Maingot had reported his favorable results in the use of esophagocardiomyotomy or the modified Heller procedure. This operation, performed through the infradiaphragmatic approach, consisted of a long myotomy extending well down over the anterior wall of the stomach and exposing the mucosa of the terminal esophagus and stomach through the incision.

Since 1952 we have employed transthoracic linear myotomy as the treatment of choice in all patients operated upon for megaesophagus (Fig. 8). The transthoracic approach was used for several reasons. It was postulated that clinical failures following linear myotomy would be related directly to the length of the incision; Graham suggested in 1951 that the esophageal mucosa be exposed for a distance of 3 in., to insure interruption of the effective constricture fibers of the cardiac sphincter. There is little

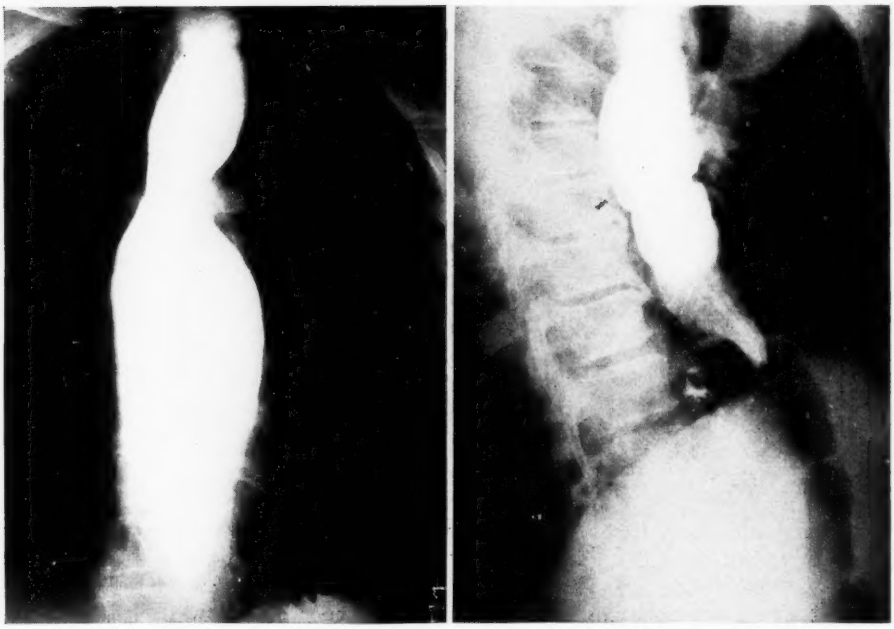


Fig. 9.—Radiographic studies in a patient with severe megaesophagus treated by linear esophagomyotomy. The postoperative picture (right) demonstrates reduction in the caliber of the esophagus and some visible return of peristalsis. Although the radiographic appearance will never resemble the normal, the patient may have complete relief of all symptoms of obstruction and retention.

reason to transect the muscular coat of the stomach, as the gastric muscularis plays little part in the obstructive mechanism associated with megaesophagus. This transthoracic modification of the Heller procedure as applied to the terminal esophagus has been uniformly successful in our experience and apparently so in the hands of others. Allison * recently made the statement that transthoracic modification of the original Heller procedure has given complete satisfaction in his series of more than 70 patients.

In our first efforts to apply the linear myotomy over the distal quarter of the esophagus, a stab wound was made in the anterior wall of the stomach and a finger introduced through the cardia as a guide in severing the muscle and exposing the underlying mucosa. This embellishment has since been abandoned, and we believe it to be entirely unnecessary. A Levine tube is introduced into the lower esophagus the day before operation and is used to clean out retained food elements. At the time of surgery it can be guided through the intact junction of esophagus and stomach and used for postoperative decompression. With blunt surgical scissors the hypertrophic and gritty circular muscle may be easily cut under direct vision to expose the underlying mucosa. As the fibers are separated, the relieved mucosa pouts into the incision in much the same manner as the pyloric mucosa is seen during a Fredet-Ramstedt procedure. Care is taken to divide all fibers of the circular muscle; an intact band at the junction of esophagus and stomach may leave residual constriction and permit herniation of the exposed mucosa to form an epiphrenic type of diverticulum. With good exposure and careful dissection this possibility is easily averted. It is our practice to continue the incision well up the

* Allison, P. R.: Personal communication to the author.

esophagus for a distance of 8 to 12 cm. As stated above, the inflammatory changes in the mucosa suggestive of peptic esophagitis are rare, and a cleavage plane between the hypertrophic muscularis and the mucosa is easily developed. For this reason mucosal perforation is rarely encountered; should it occur, a simple fine nonabsorbable surgical (silk) suture will suffice to correct the defect. The hypertrophic muscularis will contain well-developed blood vessels, and fine silk ligatures are usually employed to maintain hemostasis as vessels are divided. At the completion of the operation the Levine tube is left within the stomach, and decompression is maintained for several days after surgery. Usually these patients are able to partake of a normal house diet by the fifth or sixth postoperative day.

On occasion we have encountered an element of megaesophagus related to short esophagus. In these patients dysphagia was a predominant symptom; pain and heartburn produced by gastritis within the thoracic stomach were of secondary importance. The favorable results associated with megaesophagus have encouraged us to employ complementary myotomy when transthoracic repair of the short esophagus is performed. Relief of the dysphagia has been uniform when linear myotomy has been combined with repair of short esophagus. We believe it to be a worth-while adjunct in this type of disease.

PRIMARY RESECTION

In 1951, Wangensteen described an operation which was considered a physiologic approach to megaesophagus. The operation is extensive; the terminal esophagus as well as the upper stomach is resected, with a direct anastomosis between the esophagus and the gastric remnant. This is not the first effort designed to relieve the symptoms of megaesophagus by resection and anastomosis, but it is probably the most aggressive. In our opinion, it is a procedure that is far too radical, considering the benign nature of the underlying disease and the uniformly excellent response to simple myotomy. We have not employed Wangensteen's operation, and there is little likelihood that we shall.

SUMMARY

Megaesophagus is a distinct disease entity quite different from achalasia or functional cardiospasm. It is a disease characterized by tonic contraction of the circular muscle of the terminal esophagus and proximal dilatation of part or all of this organ.

Whereas the exact causes are not known, the basic disturbances in physiology are apparent. Dysphagia, secondary to the contraction of the hypertrophic inferior constrictor muscle, and food retention are the major clinical features of the disease.

Treatment by linear esophagomyotomy offers prompt and lasting relief of symptoms.

In this series 32 patients have been treated surgically; 12 were treated by esophagocardioplasty, and all but 3 required a secondary operation. The 20 patients who were treated by transthoracic linear myotomy have obtained complete relief of dysphagia and food retention.

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Congenital Anomalies of the Esophagus

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None of the congenital anomalies offer a greater challenge than those of the esophagus. Though steady progress has been made in this field, much remains to be accomplished. Diagnosis must be made earlier; surgical treatment must be improved; preoperative and postoperative care must be better managed if the high mortality is to be reduced to a satisfactory rate.

In 1670, Durston* recorded the first instance of a simple atresia of the esophagus. Thomas Gibson, of London,† in 1696 described atresia of the esophagus with tracheoesophageal fistula. During the following 232 years, only 132 verified cases of the anomaly were reported. Current experiences, based particularly upon findings at rather large children's hospitals, suggest that congenital lesions of the esophagus occur once in each 2500 births, a rate approximately the same as that for imperforate anus.

In 1929, Vogt [3] suggested a good working classification of congenital esophageal atresias. Holinger [4] presented a more comprehensive classification in 1951. With a few minor modifications it is as follows:

I. Anomalies of esophagus only
   - Absence, duplication, webs, and stenosis
   - Short esophagus and achalasia
   - Atresia without fistula

II. Combined esophageal and tracheal anomalies
   - Atresia of esophagus with tracheoesophageal fistula
   - Tracheoesophageal fistula

III. Esophageal complaints caused by other anomalies
   - Vascular rings and anomalies of other organs

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* Quoted by Mackenzie.[1]

† Quoted by Plass.[2]

ANALYSIS OF CASES

This review of congenital anomalies of the esophagus included all those encountered over a period of 15 years.

There were a total of 90 patients admitted to this hospital in whom the diagnosis of a congenital lesion of the esophagus was made. The frequency of the lesions encountered is set forth in Table 1. They may be divided into two general groups. The first group, or 13.3%, is composed of the duplication, stenosis, cardiospasm of the esophagus, and atresia without fistula. The second group, or 86.7%, consists of tracheoesophageal fistulas (8.9%) and the atresias with fistula (77.8%). It is apparent that with each successive five-year period a greater number of esophageal lesions have been studied.

During the entire 15-year period there were only six patients with congenital anomalies of the esophagus who were not treated. In the first five-year period two of these patients were not operated upon because of prematurity or overwhelming pneumonia. In the second five-year period three of these patients were acutely ill and died in less than 18 hours after admission to the hospital. In one patient it was not possible to establish the diagnosis of suspected tracheoesophageal fistula, though this was proved correct by autopsy some three months later. During the third five-year period all infants were operated upon, irrespective of age and size. One infant weighed only 3 lb. 8 oz.

The average size of these infants and the delay between the birth date and hospital admission is given in Table 2. The average weight of the infants has not changed appreciably with the passage of time. Though

TABLE 1.—*Analysis of the Congenital Esophageal Anomalies*

		Duplications	Stenoses	Cardiospasm	Atresia Without Fistula	Fistula	Atresia With Fistula	
I.	1940	..	..	..	..	..	1	
	1941	..	..	..	..	..	0	
	1942	..	..	..	..	..	1	
	1943	..	..	..	..	..	4	
	1944	..	..	..	..	..	2	
II.	1945	..	..	..	..	..	2	
	1946	..	..	1	2	..	4	
	1947	..	..	..	..	1	4	
	1948	..	..	..	..	..	5	
	1949	1	..	..	2	1	8	
III.	1950	..	..	..	..	2	10	
	1951	..	1	1	..	..	8	
	1952	..	..	..	1	1	5	
	1953	..	1	1	..	1	9	
	1954	..	..	..	1	2	7	
	Total	1	2	3	6	8	70	90
	% of Total	3.3%		3.3%	6.7%	8.9%	77.8%	
		13.3%				86.7%		100%

TABLE 2.—*Average Weight and Age at Hospital Admission*

Period	Wt. Average	Age at Adm.
I. (1940-1944)	6 lb.	5 days
II. (1945-1949)	6 lb. 3 oz.	3.9 days
III. (1950-1954)	6 lb. 4 oz.	2.6 days

prematurity increases the risk, it is not regarded as a contraindication to surgery. The first successfully treated patient in this series weighed only 4 lb. 12 oz. at birth. During the last five-year period, four of six infants ranging in weight from 4 lb. 6 oz. to 5 lb. 8 oz. survived. There has been a progressive decrease in the delay between the date of birth and the time of hospital admission. Although during the last five-year period the average age at the time of admission was 2.6 days, there were several unusual delays. One infant admitted on the eighth day of life survived treatment, contrary to the usual experience.

Additional congenital anomalies were discovered in 12% of the patients studied. These anomalies were imperforate anus (five), duodenal atresia (one), cyanotic heart disease (three), and skeletal deformities of the spine and extremities (two). Although imperforate anus is a serious lesion in itself, each of these five patients survived both the repair of their atresia of the esophagus and the repair of the imperforate anus.

As recorded in Table 1, duplication of the esophagus, congenital stenosis, and cardiospasm account for only 6.6% of the lesions reviewed. These lesions were treated by standard surgical procedures without fatality and will not be considered further.

Although the surgery for a tracheosophageal fistula and that for an atresia without or with a fistula are similar, it is proper that the survival rate for each group be considered separately (Table 3). It is readily seen that atresia of the esophagus without a fistula continues to have the lowest survival rate of the lesions studied; none of the six patients lived. Atresia of the esophagus with fistula is a more favorable lesion. The survival rate for patients with these lesions during the last five-year period was 66.6%. Tracheoesophageal fistula is the most favorable anomaly of all. There was no surgical mortality in this group. Although there are two deaths recorded, one was a patient in whom a lesion was suspected but who was not operated upon. The second patient died of congenital heart disease following the repair of its esophageal defect.

Complications in the group of surviving patients included a leak at the suture line of the esophagus necessitating mediastinotomy in four patients; all survived. By far the commonest complication was stricture. Evidence of stricture developed in two-thirds of the

TABLE 3.—*Survival Rate*

Period	Atresia Without Fistula		Tracheoesophageal Fistula		Atresia with Fistula	
	No.	Per Cent Surviving	No.	Per Cent Surviving	No.	Per Cent Surviving
I. 1940-1944	0	0	0	0	8	0
II. 1945-1950	4	0	2	50% (1) corrected	23	34.7% (8) corrected
			1*	100% (1)	21†	38% (8)
III. 1950-1954	2	0	6	83% (5) corrected	39§	66.6% (26)
			5‡	100% (5)		

* One patient not operated upon because diagnosis could not be established.
† Two patients not operated upon because hospital residence was less than 18 hours.
‡ One patient died because of cyanotic heart disease.
§ All patients operated upon.

patients. Gastrostomy and an indwelling nasogastric string and retrograde dilatations have virtually solved this problem; the period of dilatation has varied from a total of 3 to 12 months.

Of the 42 patients who died during this 15-year period as the result of an anomaly either without treatment or with treatment, autopsies were obtained in 38. Four succumbed to a mediastinal infection resulting from an unrecognized leak at the suture line. Pulmonary edema, atelectasis, and pneumonia were the predominant findings in the remaining patients.

DIAGNOSIS

The diagnosis of most of the congenital esophageal lesions can be easily established. These newborn infants usually have difficulty in breathing or have an excess of mucus in the mouth and pharynx. There is difficulty with the first attempt at nursing, with symptoms of choking and cyanosis. In a few instances abdominal distention may be the only abnormality noted. In any child with such symptoms a certain minimum number of diagnostic procedures should be carried out.

A soft red rubber catheter should be passed by way of the mouth into the esophagus. This type of catheter is desirable because it is radiopaque. If an obstruction of the esophagus is encountered, further corroborative evidence is needed to establish the diagnosis of atresia or stenosis. Even though a normal lumen of the esophagus is demonstrated, further studies may be indicated.

The roentgenographic study of the child should include the passage of the catheter into the esophagus under fluoroscopic vision. The observation of any obstruction can be further substantiated by the introduction of a few drops of iodized oil into the esophagus, though this is not often necessary. An obstruction in the esophagus at a level corresponding to the second to fourth thoracic vertebrae is indicative of an esophageal atresia (Fig. 1*A*). An obstruction below this level is indicative of a stenosis of the esophagus or cardiospasm and may be so demonstrated with iodized oil (Fig. 2).

A roentgenogram of the entire infant should be secured. This film not only affords an evaluation of the chest and mediastinum (Fig. 3) but also offers important information about the gastrointestinal tract below the level of the diaphragm. Gas in the intestinal tract in the presence of an atresia of the esophagus is indicative of a coexistent tracheoesophageal fistula (Fig. 1*A*), whereas the absence of a gas pattern means the absence of a fistula. This is a fact of utmost importance in planning the surgical approach for these infants. In addition, an abnormal intestinal gas pattern may clearly indicate other associated abnormalities, such as duodenal atresias, jejunal atresias, or imperforate anus.

Particular attention should be given to the infant in whom there has been demonstrated an esophagus with a normal lumen but in

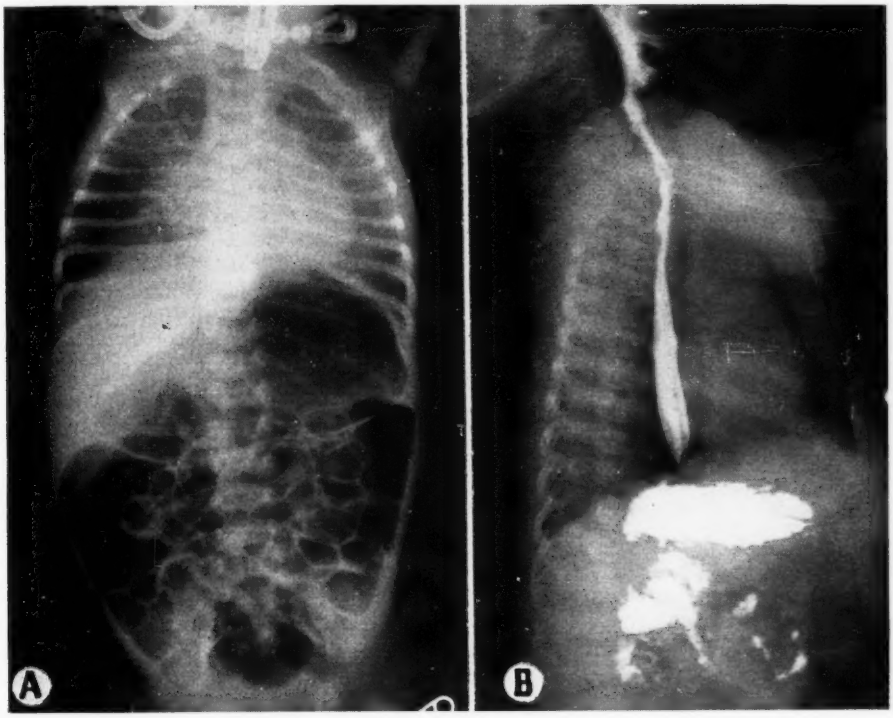
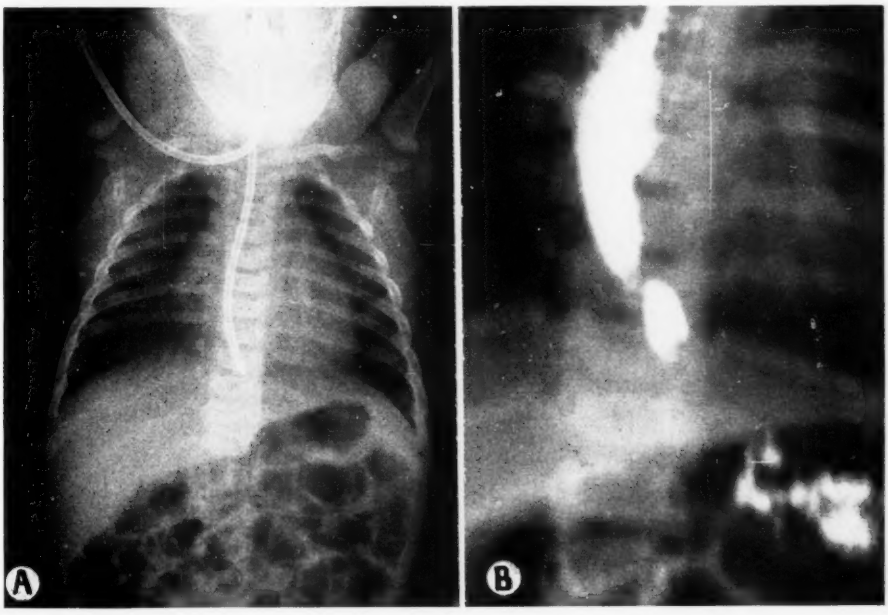


Fig. 1.—*A*, atresia of esophagus with fistula. Catheter demonstrating the atresia. *B*, postoperative film of esophagus.

Fig. 2.—*A*, stricture of esophagus with catheter in esophagus. *B*, iodized oil demonstrating stricture.



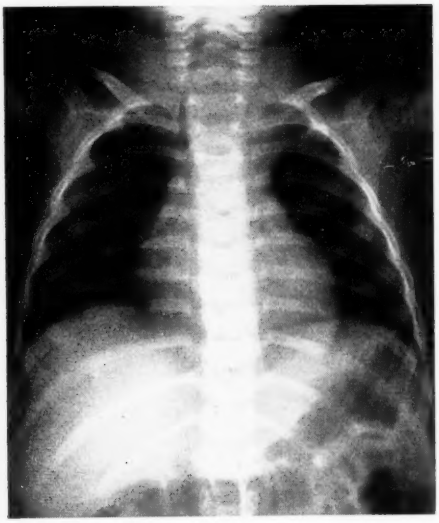


Fig. 3.—Duplication of esophagus demonstrated as mediastinal mass.

whom there is evidence, both clinically and roentgenographically, of an excess amount of air in the stomach and remainder of the small and large bowel. A tracheoesophageal fistula (Fig. 4) should be considered when these conditions exist. Opaque media may be used in an attempt to demonstrate such a fistula by introducing the iodized oil into either the esophagus or the trachea, but in our experience this maneuver has not demonstrated a fistula with any degree of accuracy. Though endoscopy is seldom used, it is particularly valuable in suspected cases of tracheoesophageal fistula. The significant observation during esophagoscopy is the escape of air from the trachea through the fistula and into the esophagoscope with each respiration. This escape of air often sounds similar to the passage of flatus from the rectum. This finding is present as long as the esophagoscope is above the fistula and is not observed when the esophagoscope is below the level of the fistula. This abnormal escape of air is a very reliable diagnostic aid; however, the fistula itself is seldom seen.

TREATMENT

Duplications of the esophagus present no particular problem, inasmuch as they are treated easily by excisional therapy. The stenoses and cases of cardiospasm may be more difficult, but they generally respond well to plastic surgery procedures or retrograde dilatations.

Atresia of the esophagus without fistula probably should ordinarily be treated by multiple-stage procedures, using such structures as colon, jejunum, or stomach to reconstruct the esophagus.

Since the esophageal atresias with tracheoesophageal fistula and the tracheoesophageal fistulas constituted 86.7% of the entire experience, the management of these conditions will be discussed in some detail.

Preoperative Care.—The preoperative care of these patients is demanding and best supplied by special nurses. Too often a delay in diagnosis has already resulted in aspiration pneumonia, atelectasis, and dehydration. On admission the infant is placed in oxygen. The pharynx should be aspirated of mucus as often as necessary with gentle suction through a soft rubber catheter. Ade-

Fig. 4.—Tracheoesophageal fistula demonstrating distention of stomach and bowel with gas.

quate doses of penicillin are given when pneumonia and atelectasis are present. When dehydration is evident, intravenous fluids are given through a small polyethylene tube in the saphenous vein at the ankle, preferably the left, since the infant will be lying on this side at the time of surgery. Whereas the normal infant requires 60 to 75 cc. of fluid every 24 hours for each pound of body weight, these patients are best managed by limiting fluids to 40 to 50 cc. a pound for the same period of time. Too much fluid, especially saline solution, may produce pulmonary edema, which is difficult to manage. Blood transfusions are rarely given to these infants in the preoperative period, as their hemogram usually indicates an abnormally high hemoglobin level. However, a blood transfusion is advisable during surgery. The amount of blood used is the equivalent of 10 cc. of blood for each pound of body weight.

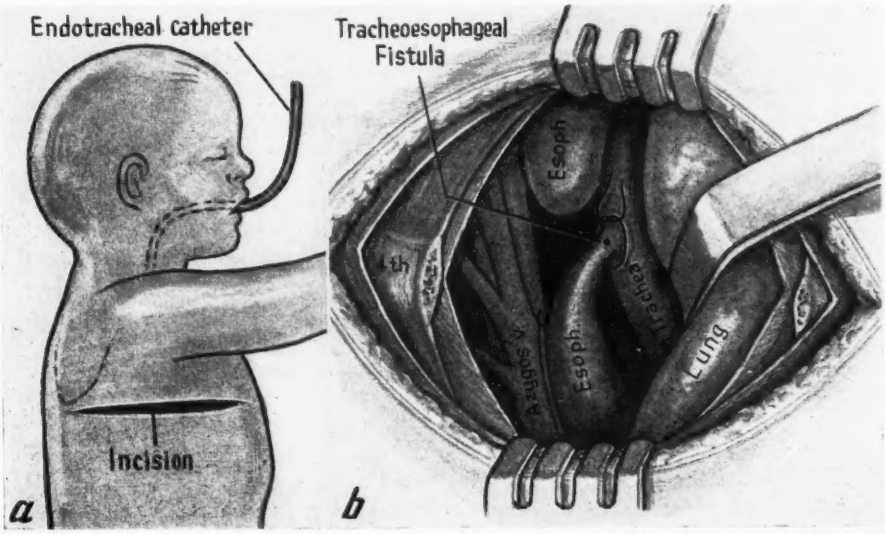
As suggested by Bigger,[5] a preliminary gastrostomy is not made routinely; however, on two occasions with extreme gastric distention a preliminary gastrostomy proved very helpful.

Surgery is seldom planned for these infants as an emergency procedure. The operative procedure on the esophagus is usually carried out on the day following admission to permit adequate preoperative preparation.

Operation.—Anesthesia has not proved difficult. Prior to 1947 local anesthesia and open mask anesthesia was used with moderate success, but since the routine use of a general anesthetic and endotracheal intubation there has been no real problem. Not a single patient has developed laryngeal edema that required a tracheotomy.

The original right parascapular incision with subperiosteal resection of posterior segments of three or four ribs, as proposed by Haight,[6] was used in my early experience. However, Bigger's[5] suggestion of subperiosteal resection of only one rib has given good surgical exposure and has eliminated paradoxical movements of the chest during the postoperative period (Fig. 5*A*). A retropleural dissection is used to approach the mediastinum. With reasonable care the danger of perforating the pleura is not great. It is felt that the advantage of an intact

Fig. 5.—*A*, position of infant and incision illustrated. *B*, retropleural exposure with excision of 4th rib.



pleura is desirable (Fig. 5*B*). A division of the azygos vein gives wide and adequate exposure of the esophagus.

In cases of tracheoesophageal fistula the esophagus is dissected free from the trachea. The fistula is usually found at a level well above the carina. The fistula is ligated with a transfixed 0000 nonabsorbable surgical (silk) suture flush with the trachea, and the fistula is divided. The esophageal defect is then easily closed with interrupted 00000 nonabsorbable surgical (silk) sutures.

It is necessary to free the esophagus from its fibrous attachment to the trachea sufficiently to permit its descent to meet the lower segment of esophagus with as little tension as possible. A small curved clamp is placed obliquely across the lower segment of esophagus close to the point of ligation of the fistula. The oblique direction increases the size of the lumen of this segment of the esophagus. The lower segment of esophagus is then severed and the curved clamp used to control it. Two sutures are then placed

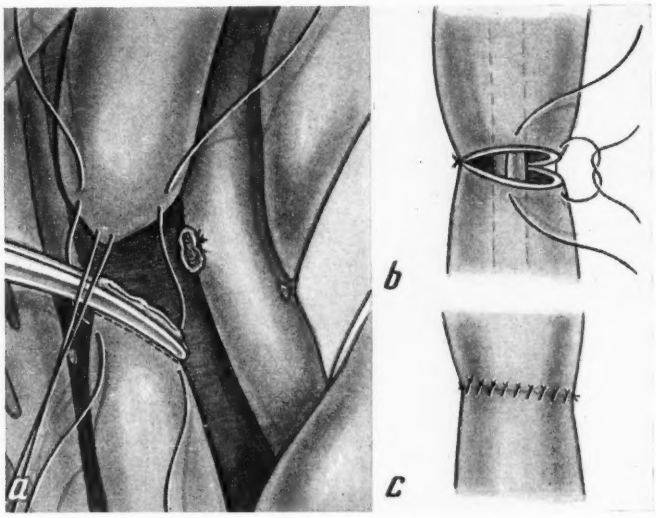


Fig.6.—*A*, method of controlling esophageal segments for anastomosis. *B*, catheter in place as anastomosis is started. *C*, anastomosis complete and catheter removed.

In an esophageal atresia with a tracheoesophageal fistula, the surgical procedure is more extensive. The distal esophagus is easily found and dissected free. The fistula is oftenest at the level of the azygos vein. The vagus nerve often will assist in locating the distal esophagus, if it is not easily identified. The esophageal fistula with the trachea is isolated and ligated with a transfixed nonabsorbable surgical suture of 0000 silk (Fig. 5*B*). The proximal end of the esophagus is anchored by a traction suture. If the pouch is not readily identified, a catheter can be passed down through the mouth to identify the proximal esophageal segment. in the two segments of esophagus and gently tied to approximate them (Fig. 6*A*). The proximal pouch is then opened and a small disc of muscularis and mucosa excised. The cuff of crushed esophagus on the lower segment is excised, and a catheter, size 10F, is passed by way of the mouth down the esophagus into the stomach. A third suture (Fig. 6*B*) is then placed and tied, after which the anastomosis of the esophagus is completed with 00000 nonabsorbable surgical sutures (Fig. 6*C*).

Drainage of the mediastinum is not established, as it is believed that the intact pleura has a better opportunity to adhere to the

repaired esophagus and to aid in sealing any minor leaks that may be present.

The lung is reexpanded fully; the pleura is inspected and the chest wall is closed. The nasogastric tube is then removed.

Postoperative Care.—The infant is placed in an oxygenated crib. The pharynx should be aspirated as often as necessary until the infant learns to swallow its saliva. Hydration is continued by the intravenous route.

On the day following the repair of the esophageal defect, a gastrostomy and insertion of a nasoesophagogastric string is done as a routine procedure for all patients (except those with simple tracheoesophageal fistulas). Twelve hours later all fluids and formula are given through the gastrostomy tube.

Oral feedings are withheld until the integrity of the esophageal anastomosis is known. The infant is taken to the x-ray department on the fourth or fifth postoperative day, where, under fluoroscopic vision, a small amount of iodized oil (Lipiodol) is placed into the esophagus. If there is no evidence of a leak, oral feedings are started, first of water, then of formula. In all instances the infants are encouraged to take their feeding by the oral route and the gastrostomy tube used only as a supplementary route, should the infant become too fatigued from nursing.

If, on the other hand, there is evidence of a leak at the suture line, all feedings are continued by the gastrostomy route. The posterior portion of the previous thoracotomy wound is then opened, and mediastinal drainage is established and maintained until the fistula closes.

It is believed that between the second and third week after the esophageal repair, gentle retrograde bougienage should be carried out to determine the size of the esophagus. If there is evidence of stricture, retrograde dilatations are continued as needed. After sufficient time has elapsed to demonstrate an esophagus of adequate lumen, the endoscopic string is removed and the gastrostomy closed.

COMMENT

The third group of Holinger's [4] classification is not considered in this review. From the 90 cases studied, it is apparent that the lesions of Group I are relatively rare when considered individually, with the possible exception of atresia of the esophagus without tracheoesophageal fistula (6.7%). The Group II lesions are by far the commoner. Atresia of the esophagus with tracheoesophageal fistula is the most frequently encountered anomaly (77.8%). Though uncomplicated tracheoesophageal fistulas occur less frequently (8.9%), their early diagnosis and proper treatment are important.

The two diagnostic procedures, esophageal intubation and x-ray of the entire infant, have been adequate to establish the diagnosis for most of the lesions encountered. For the last five years, in an effort to decrease the amount of aspiration and possible lipoid pneumonia, iodized oil has been used only when a stenosis or cardiospasm has been suspected. Endoscopy of the esophagus has been the most helpful single aid when a tracheoesophageal fistula has been suspected.

The surgical approach for all of Group II lesions and a part of Group I lesions should be the retropleural dissection. Though some use an intrapleural exposure, it is my feeling that an intact pleura is important. One advantage of an intact pleura is that it can act as a patch over the suture line of the esophagus and aid in sealing any minute leaks. If a leak does occur at the suture line, the intact pleura acts as a barrier so that an empyema does not necessarily develop. The wound is closed without drainage.

The single procedure of a primary anastomosis of the esophagus has been carried out almost without exception for the atresias with fistula. Multiple stage operations probably should be used more frequently, especially when there is a wide distance separating the two esophageal segments. When this condition is present, the patient should have the fistula closed and a reconstruction of the esophagus started. In a limited experience, the colon has proved to

be a very good structure for a substitute esophagus.[7]

The goal of all esophageal surgery is the absence of stricture formation at the line of suture. That this goal has not been achieved is suggested by the various types of anastomosis recommended for the repair of these congenital esophageal defects. As a precautionary measure for the treatment of a possible stricture and to permit early feeding, a gastrostomy is performed and an indwelling string placed in the esophagus to permit retrograde dilatations as necessary. It is recognized that at times complications result from a gastrostomy, but these disadvantages are far fewer than are the advantages for the patients who do need dilatations.

SUMMARY

In a period of 15 years, 90 congenital lesions of the esophagus have been reviewed.

The lesions encountered were

I.	Duplications	1	3.3%	
	Stenosis	2		
	Cardiospasm	3	3.3%	
	Atresia without fistula	6	6.7%	
II.	Tracheoesophageal fistula	8	8.9%	86.7%
	Atresia with fistula	70	77.8%	
	Total	90	100%	

The methods used for the diagnosis and treatment of the Group II lesions of the suggested classification are discussed.

The lesion most frequently encountered was atresia of the esophagus with a tracheoesophageal fistula. Of 39 patients treated during the last five years, 26 have survived (66.6%).

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DISCUSSION

On Papers by Drs. Donald B. Effler and James W. Rogers and J. S. Battersby

Dr. Cameron Haight, Ann Arbor, Mich.: I would like to compliment the two essayists on their very interesting presentations and on their significant contributions. As Dr. Battersby has asked me to discuss his paper, my remarks will be entirely limited to the subject of congenital lesions of the esophagus, which he has presented. He has given a thorough and comprehensive review of the types of esophageal anomalies that are encountered. As the most frequent of these are atresia of the esophagus with and without tracheoesophageal fistula, my remarks will further be limited to that aspect of his paper.

I would particularly like to mention the antibiotic coverage which one uses for these patients in conjunction with the operation. Although we noted a slight improvement in our results when penicillin was first available, the change was not a significant one. When streptomycin was added, in 1947, we noted a further improvement but not to the extent that we would have expected.

We then began a more extensive program of culturing the organisms obtained from the nose and throat preoperatively and from secretions that were present at the site of the small drain that had been inserted extrapleurally at the time of operation. All too often we found the patients had organisms that were resistant to both penicillin and streptomycin. As organisms of the Pseudomonas group were rather frequently found, polymyxin B sulfate was used in addition to penicillin and streptomycin. The results have improved considerably since then, and we find that with the present triple antibiotic coverage there is a smaller incidence of leakage of the anastomosis than was formerly encountered.

Dr. Battersby has mentioned the use of a radiopaque catheter for establishing the diagnosis and he has importantly emphasized that, if contrast material is used, only a few drops of iodized oil (Lipiodol) should be instilled. Especially if too great an amount of iodized oil is used, as had often been the case as seen in the preadmission x-rays, one sees considerable spill-over of the contrast material in the bronchial tree. In an endeavor to lessen this objection to iodized oil, we have for several years used sodium acetrizoate (Urokon) in

small amounts as the contrast material, if any should be believed to be needed.

Differences of opinion exist regarding the advisibility of gastrostomy as a feeding measure during the immediate postoperative convalescence. As we have had several unfortunate deaths from gastrostomies in the past, we do not customarily use a gastrostomy at the present time. Instead, the infants are fed for the first week or so by means of a polyethelene tube inserted at the time of operation. Our present indications for gastrostomy are leakage of the anastomosis and postoperative stricture so tight that retrograde dilatations are required, and gastrostomy is used as a feeding measure in those patients without air in the stomach before operations and for those in whom immediate restoration of esophageal continuity is not undertaken.

In regard to the operative technique, we prefer the extrapleural approach as does Dr. Battersby. We do not, however, divide the azygos vein unless this is essential. Instead, it is rolled forward and downward after dividing its highest intercostal tributaries. A layer of fascia is intentionally allowed to remain attached to the uppermost margin of the azygos vein. After completion of the anastomosis, this layer of fascia can usually be used as a layer to cover the anastomosis.

I should like to present a follow-up of our first survival of a patient with esophageal atresia and tracheoesophageal fistula following primary esophageal anastomosis. She was admitted 13 days after birth, and, although she had been brought a long distance from the northern peninsula of Michigan by automobile, her fluid requirements had been maintained by interval injections of subcutaneous fluid en route. She is now living and well, and will be 14 years of age next month.

Our results with patients with esophageal atresia are essentially the same as those mentioned by Dr. Battersby. Since 1939 we have had 169 patients with esophageal atresia; operation was performed for 160 patients and there were 94, or 58.7%, operative recoveries. Of these patients 13 have died following their initial discharge from the hospital, and 81, or 50.6%, are now living. Seventy-six of these patients have been admitted during the last five years. In this latest five-year group, two patients were not operated upon. Fifty-one, or 67.1%, recovered from the operation and were allowed to return home. Of these patients 7 have died since then, with the result that 44, or 57.8%, are now living. Somewhat more than half of the late deaths were due to causes unrelated to the operation, such as congenital heart disease and respiratory tract or gastrointestinal infections.

DR. JOHANN L. EHRENHAFT, Iowa City: I would like to make two short comments.

First, in regard to Dr. Effler's paper we have had the same experience as he did with the short side-to-side anastomosis in achalasia between the dilated esophagus and the stomach. We have operated on a series of patients using this procedure, the last one having been operated on in 1950. All of those patients had difficulty postoperatively. They all developed esophagitis due to reflux, and they either had severe bleeding due to ulceration at the esophagogastric anastomosis or some of them developed strictures at the site of anastomosis.

We reported this series of patients in February, 1951, in the *Journal of the American Medical Association* and at that time proclaimed this operative procedure more or less as a cure-all for this disease. We were entirely wrong. I think it is a very bad operative procedure. Since then we have done Heller procedures, and they are quite satisfactory.

My further remarks will pertain to the paper by Dr. Battersby. We have seen 60 patients with the congenital anomaly of tracheoesophageal fistula and atresia of the esophagus since 1937. Forty-six of those patients had operative procedures carried out. In the early cases obviously some of those procedures were palliative only and were not curative in the sense of correcting the congenital anomaly as we understand it today. During the last few years we have given up the extrapleural approach and have repaired all of the lesions transthoracically. Only about 45% of the operated patients survived. One thing stood out in a recent review of our patients. It became apparent that we have not been able to save any infants who have had extensive additional congenital anomalies, except skeletal ones and the ones with atresia of the anus. All the other patients have died. This may not be in concurrence with the experiences of others, but it is certainly a rather disappointing finding as far as we are concerned.

DR. CONRAD R. LAM, Detroit: I should like to discuss Dr. Effler's paper and to agree with him partly in regard to the extent of the Heller cardiomyotomy.

[Slide] This shows the finger inserted in the stomach, as we are carrying out the Heller myotomy. Here we have incised the diaphragm through the crural arch. After getting two postoperative diaphragmatic hernias, both of which were very unsatisfactorily repaired at secondary operations, we no longer divide the crural arch but are content to make a counter incision in the diaphragm which is rather easily closed.

If one is tempted to carry the incision down on through the muscularis of the stomach, it can be done in two stages: first, from above and, second, from below.

I should like to disagree with Dr. Effler about the name of this condition. Why should we call this

megaesophagus, naming it after a passive secondary effect, when the trouble is only in the lower one centimeter of the esophagus? As Dr. Effler has demonstrated it is due to localized spasm. I hope that Dr. Effler will be consistent and refere to pyloric stenosis as "megastomach."

DR. WILLIAM M. TUTTLE, Detroit: I heartily agree with Dr. Effler that operative procedures other than some modification of the Heller procedure have not been extremely satisfactory.

We have had two fatal hemorrhages from a side-to-side anastomosis between the fundus and the esophagus which were due to late ulceration in that area along the suture line. Such patients have constant reflux and have actually great difficulties postoperatively.

We have not used the same type of procedure which Dr. Effler has used. We have carried the incision through the muscularis of the esophagus and the serosa and muscularis of the stomach down to the mucosa of each. I do not believe that you have to put your finger in the stomach to do it. If the outer layers are carefully cut through, you should not nick the mucosa very often.

What we have done is to close the serosa to the muscularis transversely. That gives some redundancy of the mucosa in the area of the repair, with the result that the incidence of reflux is reduced.

Our experience in using the typical Heller procedure, or the anterior Heller as it is preferably called, has not been as encouraging as Dr. Effler's has been. We have had reflux. We have had this difficulty with it, and, thus, we have tried to make some sort of valve in that area for these individuals.

I would like to comment briefly on Dr. Battersby's paper, about the demonstration of a tracheoesophageal fistula. It is a difficult thing to demonstrate by x-ray, but, if a catheter is introduced into the esophagus of these babies and iodized oil is injected and then the baby is suddenly turned on its abdomen and x-rays are taken, often a good demonstration can be obtained.

The reason that demonstration is difficult by ordinary x-ray technique is the fact that the esophagus lies in the back of the trachea. Naturally, if you are going to put iodized oil in these children's esophagi, you have to turn them on their belly in order to get the oil to flow through.

We have demonstrated, within the last two or three weeks, two of these states very nicely by that technique, and it may be helpful to others.

DR. DONALD B. EFFLER, Cleveland: I appreciate very much the comments by the discussants.

All of us are in agreement that the Mikulicz principle is not applicable to this disease and is almost doomed to bad results from reflux regurgitation and also the creation of a small thoracic stomach, which we think is quite significant.

The third method of treatment has not been mentioned by the discussants. The magnitude of the operation is not justified.

As far as the Heller procedure itself is concerned, I think Dr. Lam's suggestions are certainly worth while. As a matter of fact, the "finger in the dike" technique as a guide is one we have used and have since abandoned.

Dr. Tuttle's experience is certainly parallel to ours, as is Dr. Ehrenhaft's, in that the line of cleavage between the hypertrophic muscularis and the mucosa is so sharp and clear that it is no great problem, and nicking the mucosa is a theoretical complication more than an actual one. Again, I don't believe it requires any great technical feat to stay out of the lumen of the esophagus. If it should occur, certainly one or two sutures are all that are necessary.

One thing that is extremely important is that, when you take down the cardiac end of the stomach, you incise the phrenoesophageal ligament, and so on. You do predispose toward a hiatus hernia. It is extremely important in the closure of the chest to make sure that the stomach is restored exactly the way you found it, because if you superimpose even a small hiatus hernia your results are going to be greatly hampered in the last analysis.

Actually, we believe that a long linear myotomy (and we emphasize the length of it) is extremely important and to all intents and purposes appears to be curative.

Treatment of Portal Hypertension with Hepatic Artery Ligation

An Evaluation

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W. T. McELHINNEY, M.D., Covington, Ky.
and
B. G. MacMILLAN, M.D., Cincinnati

Of the numerous surgical procedures which have been developed for the treatment of cirrhotic patients with portal hypertension complicated by esophageal varices and gastrointestinal hemorrhage, ligation of the hepatic and splenic arteries with or without ligation of the left gastric artery has received considerable attention during the past four years.

Opinions among surgeons have differed greatly as to whether or not the procedure of arterial ligation offers any lasting benefit to cirrhotic patients. The original reports of Rienhoff [1] and Berman [2] indicated that favorable results followed the procedure. In Rienhoff's series, 50% of the cases surviving hepatic and splenic arterial ligation for hemorrhage were benefited, and 11 of 13 who underwent ligation for intractable ascites were improved.

On the other hand, Madden [3] and McFadzean and Cook [4] have concluded that the operation was useless. Only one of Madden's eight cases survived hepatic artery ligation, and he therefore felt that the operation was contraindicated. The recurrence of bleeding in four of five patients after ligation led McFadzean and Cook to conclude that the procedure had no merit.

This operation was taken up by us with caution and some reserve for a number of reasons. Our early results with it were very encouraging, however, and this stimulated us to use it on 18 selected cases of severe cirrhosis.[5]

Our experiences are recorded here to add to the general information and specific data concerning the use of hepatic and splenic artery ligation in cirrhotic patients with portal hypertension.

MATERIALS AND METHODS

A total of 40 cases of portal hypertension have been treated surgically during the past seven years by members of the department of surgery of the University of Cincinnati. Eighteen of these have been subjected to ligation of the hepatic artery during the past three years ten months (Table 1). Active gastrointestinal bleeding, clinical jaundice, and biliary cirrhosis were considered to be contraindications to the procedure.

Portal cirrhosis was the cause of the portal hypertension in 15 patients and postnecrotic cirrhosis in 3. The average age of the patients was 46.7 years. Thirteen patients had varying degrees of both ascites and severe gastrointestinal hemorrhage, while four had hemorrhage only and one had ascites only. In general, the patients in our group

TABLE 1.—*Types of Ligation for Cirrhosis of Liver with Portal Hypertension*

Arteries Ligated	No. of Cases
Hepatic and splenic	9
Hepatic, splenic, and left gastric	9
Total	18

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From the Department of Surgery of the University of Cincinnati College of Medicine and the Cincinnati General Hospital

who were subjected to arterial ligation were more seriously ill and much greater risks than those treated by portocaval or splenorenal shunts.

Preoperatively, each patient received a complete physical examination and routine laboratory work as well as the following tests: BUN, prothrombin time, thymol turbidity, serum bilirubin, serum protein, sulfobromophthalein sodium (Bromsulphalein) excretion, cephalin flocculation, and x-ray examination after barium swallow. Liver biopsy specimens were obtained in all cases before or during the operation.

After the decision to use this form of treatment, each patient was given antibiotic therapy for five to seven days preoperatively, usually with penicillin and streptomycin or oxytetracycline (Terramycin). Particular attention was paid to elevating the prothrombin levels. In some instances these were as low as 32% when the patients were admitted.

The operation was performed with nitrous oxide-oxygen-ether anesthesia, through an upper midline incision. Working through the lesser omentum, the peritoneum over the superior border of the pancreas was incised and the pancreas was displaced downward to reveal the celiac axis and its retropancreatic position. Considerable difficulty was experienced in some cases in identifying and mobilizing the hepatic and splenic arteries owing to the excessive scarring, bleeding, and the friable splenic vein, which was often waterlogged by ascitic fluid. In each instance ligation of the hepatic artery and splenic artery was done with heavy braided silk at a point 1 to 2 cm. from the celiac axis. In nine of the patients ligation of the left gastric artery was done near the celiac axis at the same time or later. The pressure in the portal vein was determined before and after ligation of each of the vessels. The preligation pressures varied from 290 mm. to 460 mm. of water. A transfusion of from 2 to 11 units of blood was given during the operative procedure.

Postoperatively each patient was given supportive therapy including antibiotic therapy for 7 to 12 days.

RESULTS

A fall in portal venous pressure of 10 to 40 mm. of water occurred after ligation of the hepatic artery in those patients with initial pressures above 320 mm. After ligation of the splenic artery an additional fall of 30 to 100 mm. of water occurred promptly. No significant fall occurred after ligation of the left gastric artery.

The immediate postoperative mortality in the cases treated with hepatic and splenic artery ligations was 11.1% (Table 2). An additional five deaths occurred among the arterial ligation cases within four and a half months after operation. One of these was not related to the portal hypertension, but the remaining four were. An eighth death occurred in a patient who had developed recurrent bleeding 25 months after arterial ligation and who had then received an end-to-side portacaval shunt 19 months after ligation. He recovered and then died five months later after a massive gastrointestinal hemorrhage. A ninth death occurred in a patient in whom a portacaval shunt was done 38 months after hepatic, splenic, and left gastric artery ligation. Hepatic failure, coma, and death occurred three and a half months after the portacaval shunt. These two patients are unique in that they are the only ones to our knowledge in whom interruption of the arterial circulation of the liver was followed by a later and secondary shunt operation. Definite but weak pulsations of the hepatic artery were noted in the latter case at the time of the shunt operation. The number of deaths in the cases undergoing ligation, therefore, gives an over-all mortality of 50.0% for a three and a half year period after operation.

TABLE 2.—*Cause and Interval of Death*

Cause	Postoperative Interval
Severe shock	8 hours
Hepatic failure and coma (2)	1. 4 days 2. 38 months*
Recurrent esophageal bleeding	4 weeks
Multiple lung abscesses	6 weeks
Splenic infarction with subphrenic abscess	3 months
Hepatic failure	4½ months
Hepatic failure with generalized capillary bleeding	5 weeks
Recurrent hemorrhage	25 months†

* Patient also had portacaval shunt 3½ months before death for recurrent hemorrhage.

† Portacaval shunt had also been done in 19th month after ligation.

Recurrent hemorrhage from esophageal varices has occurred to date in six of the 18 cases (33.3%). In two it was fatal, while in the remaining four it varied from minor to moderate in severity. Generalized bleeding

TABLE 3.—*Results of Arterial Ligation in Eighteen Cases of Cirrhosis with Portal Hypertension*

Survival Period	No. of Cases	Severe Shock	Hepatic Failure	Hepatic Coma	Recurrent Bleeding	Lung Abscess	Splenic Abscess
3 weeks	2	1	..	1	..	..	..
4½ months	5	..	2	..	1	1	1
Longer	1	..	..	..	1*	..	..
Still alive	10	..	..	..	4†	..	..

* Hemorrhage recurred in 26 months.
† These patients have had two or more episodes of hemorrhage.

developed in another patient from all mucous membranes during hepatic coma caused by liver failure.

The causes of death in the arterial ligation cases are shown in Table 3. The fourth death was not related to the operation or the liver disease.

Of the 13 patients who originally had ascites and esophageal bleeding before arterial ligation, 11 survived a postoperative period of four and a half months and none of these showed a recurrence of the ascites. Six have had no further bleeding from the esophageal varices. In general, those patients surviving four and a half months after operation showed improvement of hepatic function as measured by liver profile tests.

The mortality was higher in the patients with postnecrotic cirrhosis who underwent hepatic artery ligation. All three patients with this lesion died within three months of severe liver failure.

REPORT OF CASES

The following case report illustrates one of the better results obtained in this series.

CASE 1.—A 46-year-old white man was admitted to the Christian R. Holmes Hospital on June 30, 1951, with a history of multiple episodes of upper gastrointestinal tract bleeding between 1947 and 1951. The severest of these was in February, 1951, and 6 units of whole blood was required then. He had imbibed 1 pt. of whisky and several beers daily until 1947, when he first noted abdominal swelling. A diagnosis of Laennec's cirrhosis was confirmed by liver biopsy (Fig. 1), and esophageal varices were demonstrated repeatedly by upper gastrointestinal x-ray studies.

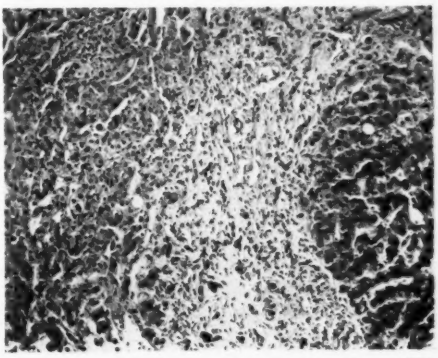
Physical examination revealed a well-developed, husky, and apparently well man whose temperature was 98.6 F, pulse rate 84, respirations 18, and blood pressure 150/95. The only pertinent physical finding at this time included a liver palpably enlarged to 5 fingerbreadths below the right costal margin. The spleen was not palpable. No other abdominal organ could be felt, and the remainder of the abdominal examination was negative except for a rather large dilated vein 15 cm. in length in the left lower abdominal quadrant. Vascular spiders were present over the chest and abdominal wall.

The admission laboratory work revealed a red-blood-cell count of 4,690,000, a hemoglobin level of 13.0 gm., a white-blood-cell count of 4350, and a differential count of 64% neutrophiles, 24% lymphocytes, 4% monocytes, and 3% stab cells. Liver function tests revealed 40% retention of sulfobromophthalein sodium in 45 minutes; thymol turbidity 2 units; negative cephalin flocculation in 48 hours; serum bilirubin prompt 0.65 mg. per 100 cc. and total 1.00 mg. per 100 cc. The total protein was 6.35 gm. per 100 cc. (albumin was 4.1 gm., globulin 2.25 gm., and the A to G ratio 1.81 : 1).

On July 2, 1951, the patient was operated upon through an upper midline incision. No free fluid was encountered. The liver was considerably larger than normal and showed a thickened capsule and marked evidence of cirrhosis with a hobnailed surface. The veins in the greater omentum were dilated, but no large or extensive varices were noted. The spleen was approximately twice normal size and showed moderate evidence of congestion.

The area of the celiac axis was approached through the lesser omental cavity. Both the splenic

Fig. 1 (Case 1).—Liver biopsy showing Laennec's cirrhosis.



and the hepatic artery were identified. Palpation of both vessels revealed a pronounced and very definite thrill along the entire course of these vessels. The hepatic artery and the splenic artery were isolated and ligated approximately 1.5 to 2 cm. distal to their points of origin. Prior to placement of the ligatures the portal pressure was measured in the omental veins and found to be 390 mm. of water. After both the splenic and hepatic artery had been doubly ligated with braided nonabsorbable surgical (silk) ligatures, the pressure was again taken and found to be 310 mm. of water. The patient received a total of 3 units of whole blood during the operative procedure and was returned to his room in good condition.

The patient's postoperative course was extremely smooth, and he was discharged without complications from the hospital on July 7, 1951. Thereafter he has enjoyed good health and full working capacity except for three minor episodes of small tarry stools. One episode occurred two weeks after discharge; the second, one year after discharge, and the final episode was two years after discharge. During the past two years the patient has had no episodes of bleeding and laboratory work performed recently reveals a hemoglobin of 14.6 gm., a red-blood-cell count of 5,130,000, a white-blood-cell count of 3550, a prothrombin time of 78%, total protein of 6.7 gm. per 100 cc. (albumin 4.1 gm., globulin 2.6 gm., and A to G ratio of 1.6:1). The liver profile shows a thymol turbidity of 3.0 units, cephalin flocculation negative in 24 and 48 hours, zinc sulfate turbidity of 6.5 units, 15% retention of sulfobromophthalein sodium in 45 minutes, serum billirubin prompt 0.15 mg. per 100 cc. and total 0.7 mg. per 100 cc., and alkaline phosphatase of 1.3 units.

After ligation of the splenic artery, shrinkage and atrophy of the spleen generally occurred. However, in one patient splenic necrosis and abscess formation followed this procedure.[6]

CASE 2.—A 56-year-old white male shipping clerk, was admitted to the Medical Service of the Cincinnati General Hospital on Aug. 9, 1951, with a history of tarry stools and hematemesis of two weeks duration. He had imbibed at least ½ pt. of whisky daily for 15 years.

Physical examination revealed a chronically ill man with a blood pressure of 125/80 and a pulse rate of 72. The pertinent physical findings consisted of innumerable spider telangiectases over the upper body, dilated abdominal veins, ascites, a nodular liver 3 fingerbreadths below the costal margin, and protuberant hemorrhoids. Esophageal varices were demonstrated on barium swallow.

Laboratory data revealed a red-blood-cell count of 3,830,000 and a hemoglobin level of 10.5 gm. His liver profile was as follows: prothrombin time 75%; sulfobromophthalein sodium retention 36.5%; thymol turbidity 10 units; zinc sulfate turbidity 23.5 units; cephalin floccculation 3+ in 24 hours; total lipids 550 mg. per 100 cc.; serum bilirubin prompt 1.75 mg. and total 4.3 mg. per 100 cc.; alkaline phosphatase 4.3 units per 100 cc.; total protein 6.30 gm. per 100 cc.; albumin 2.9 gm. per 100 cc., and globulin 3.40 gm. per 100 cc.

Under intensive medical management his cirrhosis became compensated and his bleeding stopped. He was therefore discharged on Sept. 13.

On Oct. 5 he was readmitted to the Medical Service with a recurrence of tarry stools and intermittent episodes of hematemesis. His hemoglobin level at this time was 9.0 gm. and his red-blood-cell count was 2,960,000. During the first 48 hours of his second admission he was given 3000 cc. of whole

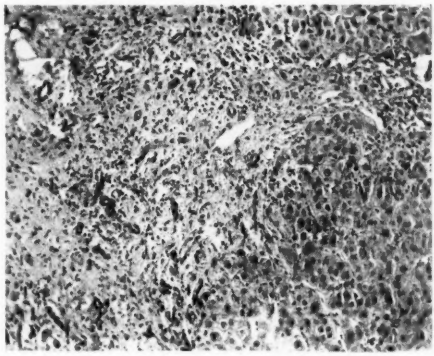


Fig. 2 (Case 2).—Liver biopsy with severe postnecrotic cirrhosis.

blood and received 16 hours of esophageal tamponade with a Sengstoken tube. His esophageal bleeding was controlled in this manner.

On Oct. 22 ligation of both hepatic and splenic arteries and a liver biopsy were performed. The liver was small, being approximately one-half its normal size, hard, and diffusely nodular. The portal pressure was found to be 275 mm. of water. Each vessel was individually isolated and ligated, the splenic 2 cm. and the hepatic 4 cm. from the sites of origin at the celiac axis. Liver biopsy (Fig. 2) revealed postnecrotic cirrhosis.

Two weeks after operation the ascites recurred, and it was again necessary to perform paracenteses once or twice weekly. The condition of the patient gradually became worse. He developed deepening jaundice and an unexplained fluctuating fever despite antibiotic therapy. His course was one of

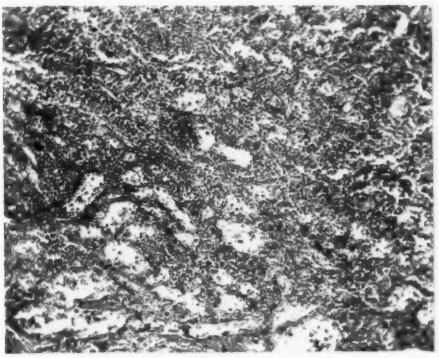


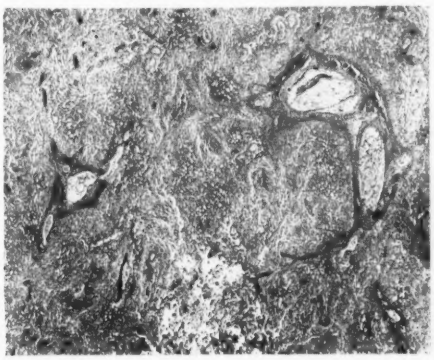
Fig. 3 (Case 2).—Section of lower pole of spleen showing viable pulp and abscess formation.

progressive deterioration, and he died eight weeks postoperatively.

At autopsy, a large abscess cavity was found in the left upper quadrant. It contained approximately 600 cc. of blood-stained purulent material, culture of which was negative. What initially appeared to be a pyogenic membrane was noted to be the capsule of the spleen. When the organ was removed, it was found to weigh 780 mg. The lower one-half of the spleen was soft with pericapsular fibrosis, and on section the splenic pulp was purplish red and appeared viable (Fig. 3). The entire upper pole of the spleen, however, had become liquefied (Fig. 4), except for fragments of pale, tannish-pink, infarcted splenic pulp varying from 5 to 15 cm. in diameter. The splenic artery was noted to be ligated 2 cm. from its site of origin at the celiac axis. Microscopic examination of the spleen showed complete infarction with numerous scattered areas of bacteria.

The ligature on the hepatic artery was noted to be 4 cm. from the site of origin, and the vessel was completely occluded at this point. The hepatic vein was patent throughout its entire course. No areas of frank liver necrosis were noted.

Fig. 4 (Case 3).—Section of upper pole of spleen showing complete infarction and partial liquefaction.



The results obtained in the patients with postnecrotic cirrhosis were disappointing. The following case is an example of the severity of the liver failure which followed hepatic artery ligation in a patient with this condition.

Case 3.—A 46-year-old white man, a known heavy drinker for many years, was first admitted to the Good Samaritan Hospital on Sept. 4, 1953, with a history of a weight loss of 60 lb. and recurrent ascites during the preceding seven months. He had had one tarry stool during this interval but denied hematemesis.

His physical examination revealed a temperature of 98.6 F, a pulse rate of 80, respirations of 24, and a blood pressure of 130/74. He appeared well developed but was poorly nourished and chronically ill. The skin and mucous membranes were icteric, and many large pulsating vascular spiders were present over the chest, face, and both arms. The abdomen was distended with fluid slightly above the level of the chest. The liver was hard and tender and extended approximately 5 fingerbreadths below the right costal margin. The spleen could not be felt.

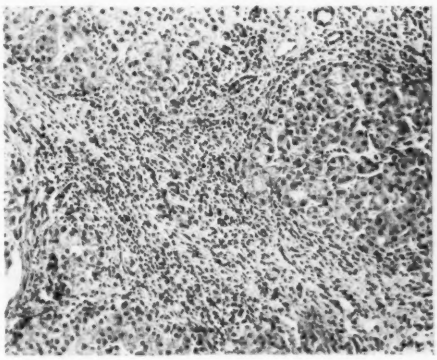


Fig. 5 (Case 4).—Liver biopsy indicating Laennec's cirrhosis.

His admission laboratory work revealed a red-blood-cell count of 4,200,000, a hemoglobin level of 12.5 gm., a prothrombin time of 90%, 7.4% of sulfobromophthalein sodium retained in 45 minutes, a cephalin flocculation of 1+ in 24 hours and 2+ in 48 hours, a total cholesterol of 693 mg. per 100 cc., albumin 3.0 gm. per 100 cc., globulin 5.5 gm. per 100 cc., with an A to G ratio of 0.54 : 1.00.

On Sept. 9, 1953, the patient was taken to the operating room, where his abdomen was explored through a transverse incision. The liver was found

to be greatly enlarged and hobnailed in appearance. The spleen was found to be only slightly enlarged. The portal pressure was found to be 290 mm. of water. The hepatic and splenic arteries were exposed through the lesser omental cavity. A definite thrill was present in both vessels. Each vessel was doubly ligated in continuity with heavy braided black nonabsorbable (silk) ligatures, approximately 2 cm. from their origin at the celiac axis. Liver biopsy (Fig. 5) revealed Laennec's cirrhosis.

The patient's postoperative course was not remarkable until Sept. 25, 1953, when he went into shock. He responded initially to transfusional therapy with a return of his blood pressure to 118/70 and a pulse rate of 96. However, on Sept. 27, 1953, he began to bleed from all orifices. Despite large quantities of blood and massive doses of vitamin K, his bleeding could not be controlled, and he died on Oct. 2, 1953.

Of particular interest have been two cases in whom previous ligations of the hepatic and splenic arteries were followed later by end-to-side portacaval anastomosis. This diverted the portal venous flow from the liver to the vena cava in patients with diminished arterial supply to the liver. Since these two cases are unique, both are presented.

Case 4.—A 45-year-old white man was admitted to St. Elizabeth Hospital on June 4, 1951. Despite a history of imbibing 1 qt. of whisky a day during the previous 15 years, he remained asymptomatic until 1947, when he first noted abdominal swelling, and the diagnosis of Laennec's cirrhosis was established. During the interval between 1947 and 1951 he had six massive episodes of upper gastrointestinal bleeding requiring 16 units of whole blood and 35 paracenteses for recurrent ascites.

Physical examination on admission revealed a temperature of 98.6 F, a pulse rate of 110, respirations of 20, and a blood pressure of 90/70. His abdomen was distended with fluid, and his liver was palpable 4 fingerbreadths below the right costal margin. Tarry stool was present in the rectal ampulla.

At time of admission his laboratory work revealed red blood cells of 1,500,000, a hemoglobin level of 5 gm. per 100 cc., a cephalin flocculation of 2+ in 24 hours and 3+ in 48 hours, and a prothrombin time of 49%. Between June 4 and June 6, 1951, he received 8 units of whole blood to maintain a hemoglobin level of 9.0 gm. per 100 cc.

On June 18, 1951, the patient was taken to the operating room, where his abdomen was exposed through a midline upper abdominal incision. His liver was enlarged and cirrhotic. His portal pressure was 300 mm. of water. The celiac axis was exposed through the lesser omental cavity, and, after the hepatic and splenic arteries had been identified, palpation of both vessels revealed a pronounced and marked thrill along their entire course. Both the hepatic and the splenic artery were then doubly ligated with braided nonabsorbable surgical (silk) ligatures 1 to 0.5 cm. distal to their origins at the celiac axis. The portal pressure following ligation of both vessels fell to 250 mm. of water. Liver biopsy (Fig. 6) revealed Laennec's cirrhosis. His postoperative course was essentially negative. He developed no jaundice and was discharged from the hospital on his 13th postoperative day.

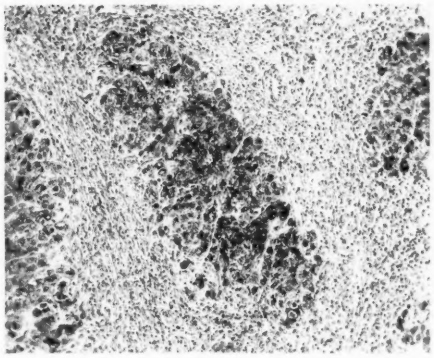


Fig. 6 (Case 5).—Liver biopsy showing far-advanced Laennec's cirrhosis.

He remained asymptomatic until December, 1952, when he again had a massive upper gastrointestinal hemorrhage for which he received 2 units of whole blood. He again remained asymptomatic, until Feb. 3, 1953, when he had a massive tarry stool, necessitating hospitalization.

On Feb. 4, 1953, the patient was taken again to the operating room, where his upper abdomen was exposed through a combined incision. The liver had become smooth and had lost a considerable amount of its previous brown nodularity. There also appeared to be some areas of regeneration. The portal pressure was found to be 100 mm. of water. A portacaval anastomosis was performed by implanting the end of the portal vein in the side of the inferior vena cava. After the completion of the anastomosis the lumen was estimated to be approximately 1 cm. in diameter. He made an uneventful recovery after this procedure and was discharged from the hospital on his 12th postoperative day. He remained asymptomatic until July 28, 1953, when he again had a massive tarry stool followed by vomiting of bright red blood. Despite intensive transfusional therapy, he had a continued downhill course and finally died on Sept. 2, 1953.

Case 5.—A 54-year-old white woman, mother of seven children, enjoyed good health until 1947, when

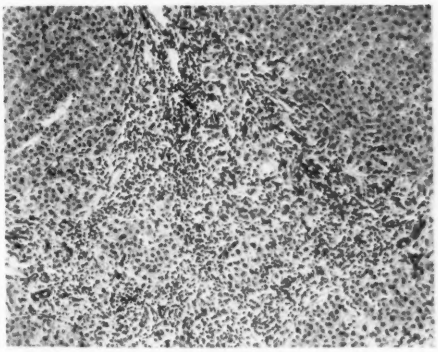


Fig. 7 (Case 6).—Liver biopsy showing postnecrotic cirrhosis and chronic pericholangitis.

she required hospitalization for jaundice associated with nausea, anorexia, acholic stools, and liver tenderness. No history of excessive alcoholic intake could be elicited.

After medical management she improved and remained asymptomatic until 1951, when she had a massive hematemesis of bright red blood again necessitating hospitalization. Because of repeated episodes of hematemesis between 1951 and 1953, she was admitted to the Good Samaritan Hospital on March 27, 1953, for ligation of her hepatic and splenic arteries.

Physical examination revealed temperature of 98.6 F, pulse rate of 100, respirations of 20, and blood pressure of 140/95. She appeared in a fair state of nutrition and was not icteric. Her abdomen was of normal contour, without evidence of fluid. The liver was palpated 3 fingerbreadths below the right costal margin and was firm and somewhat tender. The spleen was palpable 2 fingerbreadths below the left costal margin.

The pertinent laboratory data were a red-blood-cell count of 3,510,000, a hemoglobin level of 10.5 gm., a white-blood-cell count of 6200, and a differential count of 60% polymorphonuclear leucocytes, 33% lymphocytes, 3% basophiles, 3% eosinophiles, and 4% monocytes, an icteric index of 17.7 mg. per 100 cc., a direct van den Bergh reaction of 4, an indirect van den Bergh reaction of 6, a prothrombin time of 100%, a cephalin flocculation of 2+ in 24 hours and 3+ in 48 hours, and a thymol turbidity of 4.3 units. Her serum protein was 6.3 mg. per 100 cc., with albumin 3.0 gm. per 100 cc., globulin of 3.3 gm. per 100 cc., and an A to G ratio of 0.9 : 1.

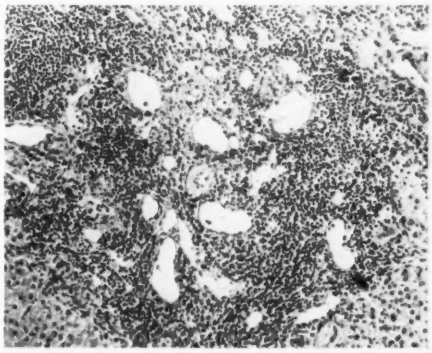
On April 14, 1951, the patient was taken to the operating room, where ligations of the hepatic and splenic arteries were performed. The abdomen was entered through a midline incision, and exploration of the abdomen revealed the liver to be enlarged and hobnailed in appearance and the spleen to be approximately twice normal size. A distinct and very marked thrill was palpable along the entire length of both the hepatic and the splenic artery. The thrill along the hepatic artery was noted to extend into the hilum of the liver. The portal pressure prior to ligation was found to be 450 mm. of water. After ligation of the hepatic and splenic arteries with double braided black nonabsorbable surgical (silk) ligatures the portal pressure fell to 320 mm. of water. A liver biopsy specimen (Fig. 7) was taken at this time and showed postnecrotic cirrhosis and chronic pericholangitis.

The patient's postoperative course was uncomplicated, and she was discharged and remained in good health until March, 1952, when she had three tarry stools. She was again readmitted to the Good Samaritan Hospital for reevaluation for additional surgery. The abdomen remained flat without evidence of fluid. There was minimal tenderness noted in the right upper quadrant. The liver was noted to extend approximately 3 to 4 fingerbreadths below the right costal margin.

Her laboratory work-up on this admission revealed a red-blood-cell count of 2,830,000, a hemoglobin level of 8.5 gm., and a white-blood-cell count of 3750. Sulfobromophthalein sodium retention was found to be 22.5% after 45 minutes, icteric index 10, prothrombin time 100%, and the cephalin flocculation 4+ after 24 hours. Total protein was 6.5 gm. per 100 cc., albumin 3.7 gm. per 100 cc., globulin 2.8 mg. per 100 cc., with an A to G ratio of 1.3 : 2.

On March 27, 1952, the patient was taken to the operating room, where the left gastric artery was exposed and ligated. This was performed through the same previous midline incision. Exploration of the abdominal cavity revealed the liver to be enlarged, but it was considerably smaller than when the patient had been operated upon one year previ-

Fig. 8 (Case 7).—Liver biopsy one year later than Figure 7 with postnecrotic cirrhosis with superimposed acute and chronic active cholangitis.



ously for ligation of her splenic and hepatic arteries. The spleen had shrunk to approximately normal size. The left gastric artery was identified and was doubly ligated with braided nonabsorbable surgical (silk) ligatures 1 to 0.5 cm. distal to its origin at the celiac axis. The liver biopsy (Fig. 8) obtained at this time showed postnecrotic cirrhosis, with superimposed chronic and acute active cholangitis. The patient's postoperative course again was not remarkable and she was discharged from the hospital on April 12, 1952. She remained symptom-free until June 17, 1954, when she again had a massive hematemesis. Upon admission to the Good Samaritan Hospital she was in mild shock. Her red-blood-cell count was 3,200,000, her hemoglobin was 7.5 gm., and her white-blood-cell count was 7450. Liver studies revealed a prothrombin time of 65%, an icteric index of 27, and 4+ cephalin flocculation in 25 hours and 4+ cephalin flocculation in 48 hours. Total proteins were 8.6 gm. per 100 cc., albumin 2.6 mg. per 100 cc., globulin 5.9 gm. per 100 cc., with an A to G ratio of 0.4:1.

She responded to esophageal tamponade and transfusional therapy, and, despite persistent icterus, her general condition improved. It was for this reason that it was thought mandatory to perform a portacaval shunt. This was done on June 8, 1954.

The abdomen was entered through a transverse incision, and the liver was noted to be greatly enlarged and nodular. Definite but weak pulsations were palpable in the hepatic artery. An end-to-side portacaval anastomosis was performed.

Her course till death, in September, 1954, was that of progressively deepening hepatic coma.

COMMENT

A study of these cases has shown that the results of hepatic and splenic artery ligation are irregular and uncertain.[7] Although it must be remembered that the cases selected for hepatic and splenic artery ligation were generally much greater surgical risks than those selected for venous shunts, an immediate postoperative mortality rate of 11.1% and an over-all mortality rate of 50% for the arterial group are significantly higher than the immediate mortality of zero and an over-all mortality of 23% in the venous shunt groups.

A recurrence of hemorrhage from esophageal varices occurred in 6 of the 16 patients (37.5%) surviving the immediate operative period of three weeks after arterial ligation. Of the original 18 cases, 6 have had no bleeding since operation 36 to 40 months ago.

McFadzean and Cook, in 1953, ligated the hepatic artery in five Chinese men with portal hypertension and esophageal varices. Of four patients followed, all had recurrent bleeding and two died. The operation failed to correct the hypersplenism which all the patients had. They concluded that the operation, therefore, was useless in the treatment of portal hypertension.

Madden, of New York, has seriously questioned the value of ligation of the hepatic and splenic arteries in the treatment of cirrhosis of the liver complicated by hemorrhage. Eight patients were treated by arterial ligation. Four died in the immediate postoperative period, one of cardiac arrest during operation, one of massive intraperitoneal hemorrhage 3 hours postoperatively, one of massive hematemesis 40 hours postoperatively, and one of anuria on the ninth postoperative day. Only one of the four patients who survived operation is living, but he has recurrent ascites and is in poor condition. One patient died seven months after operation, and autopsy showed ruptured esophageal varices but no necrosis of the liver or spleen. One patient died three weeks after operation, of hepatic insufficiency and hematemesis. Autopsy revealed no necrosis of the liver or spleen. Another patient died four months postoperatively of peritonitis. The bowel was perforated during paracentesis for recurrent ascites. A critical analysis of the results of Madden does not indicate that this procedure is necessarily not efficacious. Instead, it emphasizes the technical difficulties and dangers attending it.

Hepatic artery ligation in cases of ascites, however, appears possibly to be of importance. It is interesting to note that none of these patients developed recurrent ascites if they survived the postoperative period of four and a half months. This possibility needs further study for clarification. Similar promising results have been reported by Rienhoff and Woods[8] in the treatment of ascites.

The high mortality rate obtained in our cases of postnecrotic cirrhosis treated by hepatic arterial ligation suggests that this procedure is too hazardous for this condition. The development of severe and fatal liver insufficiency in two cases three to five weeks postoperatively, with coma, shock, massive ascites, uremia, generalized bleeding from all mucous membrane surfaces, and terminal pneumonia, is a complication which will preclude the use of hepatic artery ligation in our future cases of postnecrotic cirrhosis.

One of the three cases of postnecrotic cirrhosis, however, had been studied for six months, during which time she received intensive medical management. During this period she went into hepatic coma, but after blood transfusions her condition improved, although ascites became very severe. After arterial ligation the ascites promptly ceased, and her condition improved. She was discharged from the hospital but died six weeks later. Autopsy revealed multiple lung abscesses as the cause of death. Ascites was minimal, and the liver revealed no evidence of recent damage from the ligation, except for thrombosis of the hepatic artery.

The demonstration that two of our cases, who had undergone both hepatic arterial ligation and portacaval anastomosis in stages, survived five and six months after the later procedure indicates that the cirrhotic liver has a tremendous vascular collateral reserve. It is difficult to interpret the death of one of these patients, since she did so well for two months postoperatively and then gradually developed liver failure. It is not known whether or not the shunt contributed to the progress of the hepatic failure. There was, however, no further evidence of bleeding from the esophageal varices after the portacaval shunt.

We have been interested in the animal experiments which have been designed to disprove the efficacy of hepatic artery ligation.* One experimental study, for example, indicated that hepatic artery ligation followed by portacaval ligation caused liver coma. If sufficient time was allowed between these two operations, however, some of the animals survived.

In more recent work dogs were made cirrhotic by carbon tetrachloride. These animals were then treated by arterial ligation, usually with fatal results, this outcome being interpreted as indicative of the inadequacy of hepatic arterialization in the treatment of cirrhosis. We feel that it is very difficult to prove that the vascular aberrations of cirrhotic canine livers caused by carbon tetrachloride are the same as those seen in human livers of patients with Laennec's cirrhosis. It was also interesting that, of the seven dogs which survived the rigors of carbon tetrachloride cirrhosis, five survived hepatic artery ligation.

* References 9 and 10.

SUMMARY

Hepatic and splenic artery ligation has given sporadic and irregular results in 18 patients with portal hypertension and hemorrhage. In one-third of the cases the results have been good. Our experience has indicated, however, that this procedure carries considerably more risk than a venous shunt, in regard to both immediate and delayed mortality.

The value of excellent medical assistance in the diagnosis and treatment of patients with cirrhosis, portal hypertension, and hemorrhage from esophageal varices cannot be overemphasized.

Hepatic and splenic artery ligation with or without left gastric artery ligation has no place in the treatment of patients with active bleeding from esophageal varices, with clinical jaundice, or with biliary cirrhosis.

The presence of postnecrotic cirrhosis has been associated with a very high mortality rate in patients subjected to hepatic artery ligation and should probably be considered a contraindication to this operation.

If the operation is done, it should be reserved for patients with proved Laennec's cirrhosis complicated by portal hypertension and either ascites or a history of one or more hemorrhages from esophageal varices in whom intensive medical efforts have been

made to correct physiological and chemical alterations produced by the cirrhosis.

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Treatment of Bleeding Esophageal Varices After Splenectomy

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For many years the combination of splenomegaly, bleeding from esophageal varices, and sometimes cirrhosis of the liver was given the eponym "Banti's syndrome." It was taught that the primary disease was splenic and that disease of the liver developed subsequently. In 1936 [1] and 1937,[2] Whipple, Rousselot, and their associates confirmed the long-standing suspicion that such patients had elevated pressure in the portal venous system. In 1941 and later, Whipple * noted that cirrhosis of the liver did not develop in all such cases and that in cases in which cirrhosis was absent extrahepatic obstruction was demonstrabie in the portal system. Establishing the concept in use today, Whipple concluded that portal hypertension and its sequelae of congestive splenomegaly and esophagogastric varices develop as a result of obstruction to the outflow of blood from the portal system. He suggested that patients with this disorder be classified into two groups according to the site of the obstruction: (1) those with intrahepatic portal obstruction, due usually to the various types of cirrhosis of the liver, and (2) those with extrahepatic portal obstruction, due to changes usually in the portal vein itself, some apparently congenital, some following trauma or infection, and some of unknown origin. In addition, a few patients are seen with normal hepatocellular function and no extrahepatic portal obstruction who none the less have portal hypertension and its sequelae. The patients whom we have encountered in this last group have had livers which felt firmer and seemed to contain more fibrous tissue than is normal but which have presented no regenerative nodules or other criteria to permit a diagnosis of cirrhosis. In the present state of knowledge it is probably best to consider them as representing an unusual type of intrahepatic portal obstruction of undetermined origin.

Application of this concept of the pathogenesis of portal hypertension led the pioneer workers in the field, such as Whipple, Blakemore, Rousselot, and their associates, in New York, and Linton, in Boston, to develop operations in which venous shunts are created between the portal and caval venous systems, operations which they and others who have since become interested are still evaluating. The purpose of such shunts is to provide a direct channel for egress of portal blood which offers so little resistance to flow that use of naturally occurring collateral channels, including esophageal varices, will be minimized. It is hoped that the lowered portal pressure and lessened flow through varices will prevent serious bleeding from the varices.

For many years splenectomy was the operation most commonly used in an attempt to

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* References 3 and 4.

control bleeding from esophageal varices. Bleeding occurred after splenectomy in about half of these patients.† The present paper is concerned with treatment of these "postsplenectomy bleeders." It is largely because results after splenectomy leave so much to be desired that portacaval shunting has been receiving extensive trial. To be effective, venous shunts must be between large branches of the portal and caval venous systems. Minor shunts between small branches of the two systems are generally ineffective and tend to thrombose. The only two types of shunts which are ordinarily large enough to be worth while are the direct portacaval shunt, between the portal vein and the vena cava, and the end-to-side splenorenal shunt performed at the time of splenectomy.

Patients with intrahepatic portal obstruction have patent splenic and portal veins, except in infrequent instances when a concomitant thrombosis of the portal vein has occurred.[8] Therefore, in this group of patients construction of either a direct portacaval or a splenorenal shunt is almost always possible. In patients with extrahepatic portal obstruction the portal vein is usually thrombosed or replaced by a network of small veins, none of which is suitable for shunting. Once splenectomy alone has been performed, the splenic vein becomes thrombosed and is for practical purposes no longer available for shunting. Thus splenectomy may sacrifice the last chance to perform a suitable shunt in patients with extrahepatic portal obstruction. We agree with the many surgeons who have stressed the importance of never performing splenectomy for extrahepatic portal obstruction unless one is prepared to carry out a splenorenal anastomosis at the same time if the splenic vein is patent and sufficiently large. Factors leading to this recommendation are as follows: (1) Addition of splenorenal anastomosis to splenectomy for extrahepatic portal obstruction is rational; (2) though final appraisal of results of shunting versus results of splenectomy alone is not yet possible, results to date favor shunting, and (3) in these patients with normal livers addition of the shunt has not increased the operative mortality rate as compared with that following splenectomy alone.

Patients who have bleeding from esophageal varices after splenectomy may, like any patient with portal hypertension, have either intrahepatic or extrahepatic portal obstruction. If the obstruction is intrahepatic, that fact may be obvious when the history, clinical findings, and laboratory data support a diagnosis of disease of the liver but obscure when cirrhosis is present without the usual signs or when the intrahepatic obstruction is of the uncommon type not due to cirrhosis. In any of these circumstances the portal vein will be patent and suitable for shunting, except in the unusual instance in which a concomitant portal thrombosis exists. If the obstruction is extrahepatic, there will be no evidence for the presence of disease of the liver, and the patient may have no veins suitable for shunting or, on the other hand, may have a collateral vein in the region of the portal vein or an enlarged coronary or gastroepiploic vein of suitable size and position for shunting. Though one can be certain that direct splenorenal anastomosis will not be possible in these postsplenectomy bleeders, one cannot predict with certainty the status of veins suitable for shunting prior to exploration.

Our initial experiences with this group of patients were discouraging. In three patients who proved to have extrahepatic portal obstruction, long and fruitless explorations were performed in search of a branch of the portal system suitable for a portacaval shunt. Two of these patients, in whom no such vein was found, survived the procedure despite stormy postoperative courses, including bleeding from varices, and in these the varices in the lower part of the esophagus were later ligated transesophageally by the method of Crile.[9] The third patient, in whom a futile minor shunt was established between the right ovarian vein and a branch of the superior mesenteric vein, died postoperatively with mesenteric thrombosis, gangrene of the

† References 5 to 7.

ileum, and ascites. Temporarily abandoning any attempt at portacaval shunting in these cases, we performed transthoracic partial esophagogastrectomy on three patients who proved to have normal livers. These patients have had no further bleeding 38, 36, and 32 months postoperatively. Two of the three patients eat quite comfortably and maintain their weight; the third has a small capacity for food, complains of anorexia and heartburn, and remains underweight. Still another patient, who proved to have cirrhosis of the liver, died in hepatic coma after undergoing subtotal gastrectomy.

These somewhat heterogeneous experiences pointed to a need for a definite plan of management of these so-called postsplenectomy bleeders. Realizing that satisfactory portacaval shunts are possible in some of these patients, even some with extrahepatic portal obstruction, and persuaded by our own experiences and those of others that an adequate shunt offers protection against bleeding from esophageal varices, we returned to the idea that the first step should be to determine whether or not a large shunt is feasible.

To do this without a tedious and hazardous dissection in which a suitable vein might not be found, we have employed a laparotomy performed through a short, nearly transverse incision below and to the right of the umbilicus, which can be extended to form a right thoracoabdominal incision if the findings warrant it. Through the short incision the following steps are taken: (1) The abdomen is explored in the usual manner; (2) the liver is examined and a biopsy specimen is taken; (3) the region of the portal vein is palpated in the search for veins which may be accessible for anastomosis to the vena cava, and the presence or absence of any other large veins which might serve is noted, and (4) the superior mesenteric vein is cannulated with polyethylene tubing through a branch in the mesentery of the jejunum so that portal pressure can be measured and the portal circulation can be investigated by injecting 40 to 50 ml. of 70% sodium acetrizoate (Urokon) and taking a roentgenogram.

The presence of hepatofugal flow of blood in the portal system coupled with elevated portal pressure confirms the diagnosis of obstruction to the portal system. If the obstruction is intrahepatic, the liver is typically, though not always, grossly diseased and the portal vein is usually patent, easily palpable, quite evident on the venogram, and suitable for anastomosis with the vena cava. If the obstruction is extrahepatic, the liver is normal and the other findings can be extremely variable. Palpation of the porta hepatis may reveal a firm, hard, organized thrombus and no ballotable veins, or a soft mass of collapsible tissue which feels like a cavernous hemangioma, or sometimes a ballotable collateral vein near the free edge of the duodenohepatic ligament which feels as though it could be anastomosed to the vena cava. Occasionally a large coronary or gastroepiploic vein may be present and in such condition that it can be anastomosed to the vena cava. The portal venogram may show a network of small veins in the porta hepatis with no large channel or may suggest that a large vein is present, though perhaps accompanied by smaller veins.

In one patient a portacaval shunt was attempted only because the portal venogram indicated that two reasonably large channels were present in the region of the portal vein, despite the fact that nothing but fibrous tissue could be palpated. The veins were found with great difficulty, could not be mobilized, and were smaller than had been expected, and the rather minor shunt which was effected by means of a vein graft was followed a month after the patient's dismissal from the hospital by severe hemorrhage.

This has strengthened our resolve to demand the presence of a sizable, palpable vein before proceeding to attempt a shunt in these cases. It is realized that with this conservative attitude one might fail to attempt a shunt in an occasional case in which a shunt would be technically feasible, but one will also avoid many useless, extensive dissections which are costly failures.

If a shunt is not considered feasible, some other procedure is undertaken, usually at the same operation. Of late we have been evalu-

ating transesophageal ligation of the varices performed through a left thoracotomy incision as practiced by Crile,[9] being attracted to it by its relative simplicity and by the fact that it avoids the serious sequelae which sometimes follow esophagogastric resections.

Sixteen postsplenectomy bleeders have been encountered since this general approach to the problem was begun. Details concerning them are presented in the table. Eight underwent the simple exploratory laparotomy described above; eight did not, for various reasons which will be described. No postoperative deaths occurred in this group of patients.

Data on Surgical Treatment of Postsplenectomy Bleeding

Patient	Age, Yr.	Diagnosis: Preoperative	Diagnosis: Operative	Method of Making Final Diagnosis	Surgical Treatment	Follow-Up, Mo.	Episodes of Recurrent Bleeding
1.....	54	Cirrhosis, IHO*	Cirrhosis, IHO	Laparotomy, portal venogram	End-to-side portacaval shunt	5	1
2.....	25	Uncertain	Cirrhosis, IHO	Laparotomy, portal venogram	End-to-side portacaval shunt	8	0
3.....	31	EHO†	Cirrhosis, IHO	Laparotomy, portal venogram	End-to-side portacaval shunt	3	0
4.....	42	EHO	EHO	Laparotomy, portal venogram	Side-to-side portacaval shunt	16	0
5.....	33	EHO	EHO	Laparotomy, portal venogram	Side-to-side portacaval shunt	9	0
6.....	18	EHO	EHO	Laparotomy, portal venogram	Side-to-side portacaval shunt	12	0
7.....	27	EHO	EHO	Laparotomy, portal venogram	Side-to-side portacaval shunt with vein graft	11	3
8.....	21	EHO	EHO	Laparotomy, portal venogram	Transesophageal ligation of varices	14	0
9.....	31	EHO	EHO	Previous complete exploration	Transesophageal ligation of varices	15	0
10.....	25	EHO	EHO	Previous complete exploration	Transesophageal ligation of varices	17	1
11.....	5	EHO	EHO	Previous exploration and splenic venogram	Transesophageal ligation of varices	9	0
12.....	7	EHO	EHO	Previous exploration	Transesophageal ligation of varices	16	1
13.....	7	EHO	EHO	Previous exploration	Transesophageal ligation of varices	7	0
14.....	27	EHO	.....	Presumptive, see text	Transesophageal ligation of varices	14	0
15.....	24	EHO	EHO	Operation elsewhere	Transesophageal ligation of varices	8	0
16.....	19	EHO	.....	Presumptive only	Transesophageal ligation of varices	19	Several

* IHO: Intrahepatic portal obstruction.
† EHO: Extrahepatic portal obstruction.

If remissions afforded by Crile's procedure prove to be too few or too brief, we are prepared to turn to esophagogastric resection, perhaps of the type described by Allison and da Silva,[10] in which an esophagojejunostomy is established using the Roux "en y" technique.

Of the three patients who proved to have intrahepatic portal obstruction due to cirrhosis of the liver (Patients 1, 2, and 3), that diagnosis seemed certain preoperatively in

one, seemed uncertain but was suspected in another, and was unsuspected in the third. In each instance the short incision was extended to form a right thoracoabdominal incision and an end-to-side portacaval shunt was performed.

Of the remaining 13 patients, 5 underwent the preliminary exploration and the taking of a portal venogram described above. This procedure was not performed in Patients 9 and 10 because previous exhaustive and fruitless exploration had demonstrated that a shunt could not be made; in Patients 11, 12, and 13 because exploration at the time of previous splenectomy and splenorenal anastomosis had established the diagnosis and because it was felt that the small size of these children with extrahepatic portal obstruction made it unlikely that a suitable shunt could be established; in Patient 14 because a history of repeated widespread venous thrombosis made us fear that any manipulation of her portal venous system might predispose to further thrombosis there; in Patient 15 because an extensive exploration at another institution had failed to locate a vein suitable for shunting, and in Patient 16 because we had not developed the technique at the time when she was treated.

Fig. 1.—Portal venogram from patient whose spleen had been removed and who has extrahepatic portal obstruction. The region of the superior mesenteric vein and portal vein shows cavernomatous changes, but one fairly large vessel is visible in the porta hepatis and it was palpable. Side-to-side portacaval shunt was accomplished.

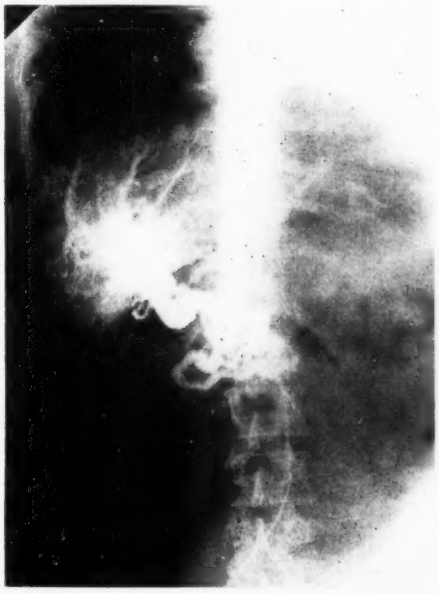

Fig. 2.—Same patient as in Figure 1. Completed side-to-side anastomosis between a collateral vein in the porta hepatis and the vena cava. Figure also shows anomalous double right renal veins.

In Patients 4, 5, and 6 satisfactory side-to-side portacaval anastomoses were accomplished. In each case a large collateral vein in the free edge of the duodenohepatic ligament was used. These veins were abnormal, thin-walled, and tortuous and received so many tributaries entering from the side facing the porta hepatis that they could not be dissected free on all sides. Thus far these patients have not bled postoperatively. A portal venogram from one of these patients is shown in Figure 1. There is a cavernomatous-looking network of veins in the region of the portal and superior mesenteric veins, with what appears to be a larger channel in the region of the porta hepatis. Hepatofugal flow in the coronary vein can be seen faintly, crossing the vertebral column. The portal pressure was 37 cm. of water. A fairly large vein could be balloted in the free edge of the duodenohepatic ligament, and it proved possible to construct a side-to-side portacaval anas-

tomosis. The vein was an abnormal collateral vein which had presumably formed in response to obstruction of the portal vein. A photograph of the anastomosis is presented in Figure 2.

Patient 7 has been alluded to above. The anastomosis made with a vein graft was a minor shunt which proved ineffective. This patient survived the operation only to bleed again three times in the following year.

Patients 8 to 16 inclusive were deemed unsuitable for shunting and underwent transesophageal ligation of the varices. In this procedure we have used Crile's technique, avoiding incision into the diaphragm to prevent interference with the normal "pinch-

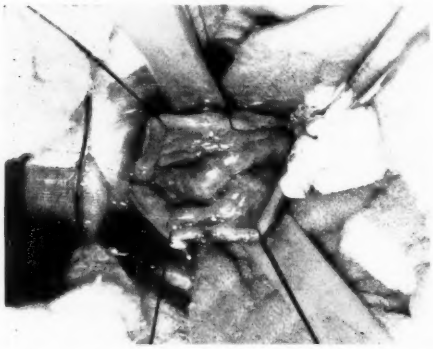

Fig. 3.—Large esophageal varices seen after the esophagus, immediately above the diaphragm, has been opened.

cock" mechanism in the hope of preventing development of regurgitant esophagitis.

A longitudinal incision about 8 cm. in length opens that part of the esophagus immediately above the diaphragm. The typical appearance of distended esophageal varices is shown in Figure 3. All visible columns of submucosal varices are sutured over and over with chromic absorbable (gut) sutures. Traction on the sutures enables one to pull gastric varices into the incision for 2 or 3 cm. and allows one to reach higher in the esophagus than the area immediately exposed by the incision. The esophagus is closed longitudinally with two rows of interrupted nonabsorbable surgical (silk) sutures. A plastic feeding tube is placed through the esophagus into the stomach and brought out through the nose. The left thoracic cavity is temporarily drained by a large catheter attached to a source of gentle suction.

In one case empyema developed postoperatively and was treated by closed drainage. Though a few patients complained of transient dysphagia soon after the operation, no symptoms related to swallowing persisted, even in the three small children. As the Table indicates, three of those patients who underwent transesophageal ligation of varices have experienced recurrent hematemesis or melena. A third patient, who had a long history of multiple venous thromboses, died of cerebral thrombosis 14 months after operation, having been without bleeding from varices in the interim. It is obvious that the period of postoperative observation is very short in all these cases.

COMMENT

The so-called postsplenectomy bleeders are a challenging group of patients. Many are young; most have normal livers. One feels that if the recurrent bleeding could be prevented, life expectancy ought to be good. The rather unorganized approach that we first took to this problem was most unsatisfying. The present approach, which takes as its goal the performance of a portacaval shunt in those in whom the operation is possible and the avoidance of dangerous, useless dissections in those in whom adequate shunts are not likely to be achieved, is logical and simplifies the problem of selecting the appropriate surgical treatment.

The choice of procedure to be done when shunts are not possible is unsettled at present. One's total experience with this problem is likely to be small, and rather than to try a few of several different procedures we decided to evaluate transesophageal ligation of varices. Our early results are described above. Crile [11] in 1953 reported that bleeding had occurred in two of nine patients with extrahepatic portal obstruction treated by this operation and followed for 6 to 45

months. In one of these patients bleeding soon after operation was followed by a remission of 33 months' duration; in the other a gastric ulcer was also present and was suspected of bleeding.

Transesophageal ligation of varices has also been used to stop acute bleeding in patients with cirrhosis of the liver. We have employed it twice under these circumstances and noted recurrent bleeding three and seven weeks later respectively. This is in harmony with Linton and Warren's ‡ larger experience, which has led them to consider the operation a temporary palliative measure rather than a definitive procedure. It is not clear why longer remissions should follow the operation when it is performed for patients with extrahepatic portal obstruction than when it is used for patients with cirrhosis of the liver, but such appears to be the case, according to data thus far available. More time and more data will be required before a final decision can be made concerning its usefulness.

SUMMARY

Portal decompression by anastomosis with the caval venous system is at present the preferred treatment for bleeding esophageal varices in patients with portal hypertension. It may or may not be possible in patients after splenectomy or splenorenal shunt has failed. The problem is one of determining whether branches of the portal system exist which are large enough and in suitable position for anastomosis to the vena cava. This cannot be done without exploration and should not involve a tedious and hazardous dissection which may be of no avail. A plan is presented whereby a brief laparotomy allows exploration of the abdomen, examination of the liver, palpatation of the porta hepatis, measurement of portal pressure, and obtainment of a portal venogram. On the basis of these data a decision is made either to attempt a portacaval shunt or to abandon this approach. The procedure of choice when a shunt cannot be done is uncertain at present. Early results of transesophageal ligation of varices are presented.

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A New Type of Portal-to-Systemic Venous Shunt for Portal Hypertension

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Surgeons today are being called upon to treat patients of all ages for portal hypertension because of its associated symptoms of gastrointestinal hemorrhage, ascites, and congestive hypersplenism. The efficacy of decompressive shunting procedures has been demonstrated repeatedly in persons with extrahepatic or intrahepatic types of portal venous obstruction.* The majority of symptomatic patients are amenable to the conventional splenorenal or portacaval shunt.

However, there remain four sizable groups of patients for whom such established procedures are impossible: (1) the "postsplenectomy bleeder" with cavernomatous changes in the portal vein itself, (2) the patient with preexistent thrombosis and recanalization of the portal vein and its major tributaries, (3) the person with excessive bleeding at surgery from periportal or perisplenic collateral vessels, and (4) the small child in whom the difficulties of obtaining an adequate-sized, patent portal-to-systemic venous shunt may be almost insurmountable. In each such case, the primary problem is that of demonstrating and dissectiing out a portal venous radicle of suitable size. With portal venography it is possible to demonstrate in such instances a dilated superior mesenteric drainage vessel or a large "blood lake" at the area of confluence of the superior mesenteric and splenic veins. Decompression of the portal system can then be accomplished by bridging the gap between the dilated portal vessel and the inferior vena cava by vein graft † or by the technique to be described.

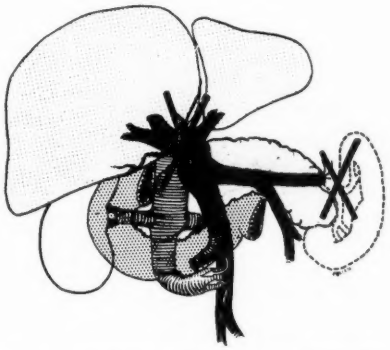

Fig. 1.—Technique for the surgical treatment of portal hypertension. A side-to-side anastomosis between the superior mesenteric vein and divided proximal inferior vena cava is depicted. This type of shunt is used in the management of patients in whom the spleen has been removed (postsplenectomy bleeder) and in whom the periportal vessels preclude dissection in this area. (Note crosses.)

In the experimental laboratory and in two clinical cases, we have performed an anastomosis between the side of the large superior mesenteric venous tributary and the divided proximal end of the inferior vena cava (Fig. 1). This has proved to be a technically feasible procedure, productive of satisfactory decompression of the hypertensive portal venous bed. This procedure is not meant to supplant the established methods of achieving portal decompression but to further

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* References 1 to 8.

† References 9 and 10.

fortify the surgeon so that he may deal more effectively, and particularly in the very young, with the mechanical problems inherent in management of this disease.

EXPERIMENTAL STUDIES

The technical problems involved in the performance of a satisfactory shunting procedure between the side of the superior mesenteric vein and the divided end of the proximal inferior vena cava have been studied in the experimental surgical laboratory.

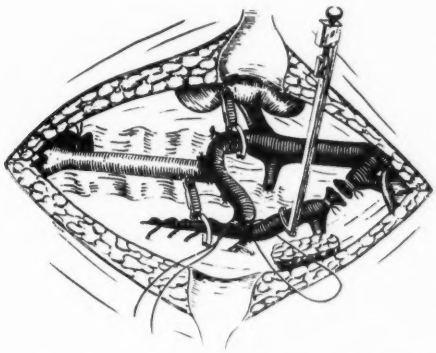


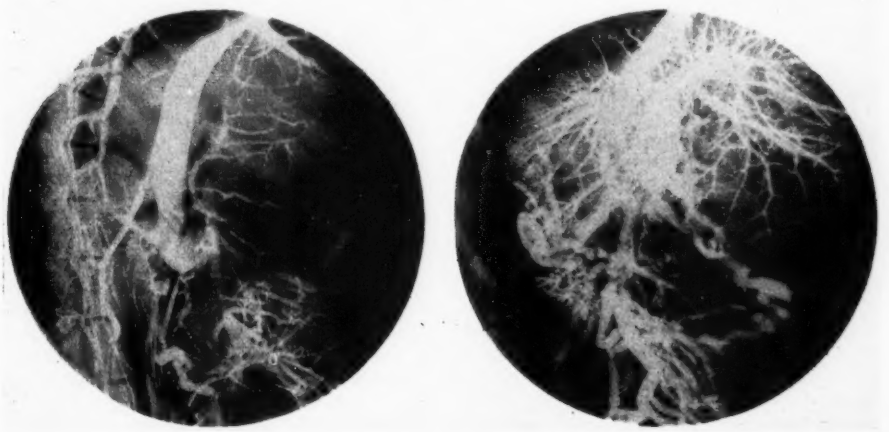
Fig. 2.—The side-to-side anastomosis between the superior mesenteric vein and the inferior vena cava as performed in the experimental animal. The portal vein has been divided.

Thirteen mongrel dogs varying in weight from 10 to 19 kg. were explored under general anesthesia through a long midline abdominal incision. After obtaining an initial portal pressure which varied from 110 to 170 mm. of saline, the superior mesenteric vein, portal vein, and inferior vena cava were dissected out of the mesenteric and retroperitoneal tissues.

The inferior vena cava was then transfixed and ligated just above its origin and the proximal end turned up into the right posterolateral side of the superior mesenteric vein. Appropriate vascular clamps were applied and an anastomosis was carried out with running over-and-over 00000 black Deknatel nonabsorbable surgical (silk) suture. The clamps were removed, and when the anastomosis was dry the portal vein was doubly ligated and/or divided below its bifurcation in the liver hilus (Fig. 2). The portal pressure after the performance of the anastomosis and the division of the portal vein varied from 92 to 150 mm. of saline. In all but one instance these portal venous pressures were less than the preshunt pressure recorded.

Eleven of the dogs survived for study; the other two succumbed to hemorrhage resulting from disruption of the anastomosis in the immediate postoperative period. In 10 of the surviving animals, a widely patent anastomosis was demonstrated at operation and autopsy examination two to six weeks later. Portal pressures were obtained at the time of death and were below the normal preshunt

Fig. 3.—Roentgenograms of the portal, hepatic, and inferior vena cava area in experimental animals: *A*, following ligation of the portal vein and performance of the shunt between the side of the superior mesenteric vein and the end of the divided vena cava. *B*, the single animal in which the shunt thrombosed. (Note tortuous channel bypassing the portal vein ligature.)



values in all but one animal. In this dog, the shunt had thrombosed but there was an anomalous pancreaticoduodenal venous radicle which effectively bypassed the portal vein ligature. The portal pressure, therefore, was elevated only to 136 mm. of saline at the time of death, as compared with 120 mm. of saline before the operative procedure, one month previously.

Roentgenographic studies of representative animals with the venous systems filled with opaque medium were obtained. The shunt was clearly visualized in each instance, and there was no evidence of dilated or tortuous collateral venous channels, except in the one animal with the thrombosed shunt (Fig. 3). The site of the anastomosis was examined and was found to have healed smoothly without thrombosis or stricture formation.

REPORT OF CASES

CASE 1.—A 7-month-old boy was admitted on May 31, 1953, to The Columbus Children's Hospital for study because of ascites, anemia, and splenomegaly. There were no prenatal or postnatal disturbances, and the child was thought to be well until one month prior to admission, when he began to pass dark diarrheal stools which were strongly guaiac-positive. At this time the spleen was found to be enlarged, and he had received a single transfusion. A few days prior to admission he developed ascites.

Physical examination revealed a well-developed and well-nourished child who was extremely pale and had obvious abdominal distention. There were no dilated abdominal wall veins. The spleen was 3 cm. below the left costal margin. Laboratory findings included a red-blood-cell count of 2,000,000, hemoglobin of 6 gm. per 100 cc.; white-blood-cell count of 7100, platelet count of 43,000, and 3.6 gm. of protein per 100 cc. of serum, with A/G ratio of 1/1. Serum van den Bergh test showed 5 mg. per 100 cc. cephalin flocculation 2+, and thymol turbidity 5.8 units. Stools were guaiac-positive.

An upper gastrointestinal radiographic examination failed to demonstrate esophageal varices. The stomach and C-loop of the duodenum were displaced anteriorly, suggesting the presence of a retrogastric mass, tentatively diagnosed as a retroperitoneal neoplasm, probably neuroblastoma. Subsequent intravenous urograms, however, demonstrated that the kidneys were not displaced. Cardiac fluoroscopy showed no evidence of pericardial effusion or constriction. The lung fields were clear.

The following day a paracentesis was performed, with the removal of 725 cc. of clear yellow fluid which contained no tumor or other cells, and total protein was 240 mg. per 100 cc. (Denis-Ayer). The bone marrow smear was hypercellular, showing impaired platelet formation and marked erythroid hyperplasia consistent with hypersplenism and chronic blood loss.

Ten days after admission, after repeated transfusions, the child was explored. The walls of the colon and small bowel were edematous and slightly cyanotic. The liver appeared normal, but the porta hepatis and gall bladder were thickened, suffused, and traversed by multiple tortuous collateral vessels. The spleen was enlarged two to three times, and there were many match-stick-sized collateral vessels in the phrenocolic and gastrolienal ligaments. The entire mesentery of the small bowel and the retroperitoneal area were tremendously thickened and filled with enlarged lymph nodes and woody edema, suggesting chronic lymphatic obstruction and producing the retroperitoneal mass described by the radiologist. The portal pressure, as measured in a dilated gastrolienal vessel, was 520 mm. of saline (above the splenic vein) (Fig. 4).

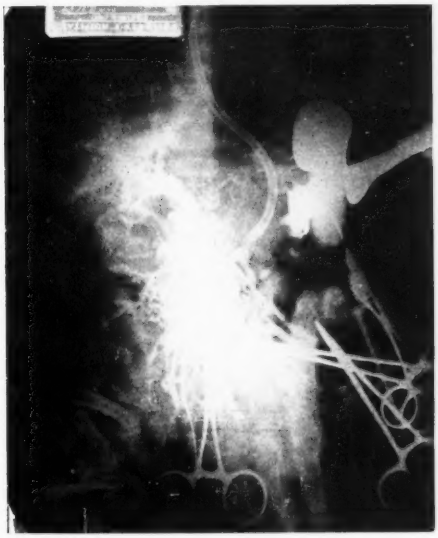
The splenic attachments were divided and the spleen and tail of the pancreas mobilized medially. A splenic vein sufficiently large to be suitable for a shunting procedure was not found. It was assumed that the portal tributaries, including the splenic vein as well as the portal vein itself, had been involved in a thrombotic process. The spleen was removed; a liver biopsy specimen was taken and the abdomen closed in layers with interrupted nonabsorbable surgical (silk) sutures.

Postoperatively, the child experienced his first episode of massive hematemesis, suggesting that the removal of the spleen and division of the collateral vessels had increased flow in the esophagogastric venous plexus. After the institution of an ulcer regimen, including oral antacid medication, his condition stabilized and he was discharged home on the 12th postoperative day, at which time his hemoglobin was 12 gm. per 100 cc. The liver biopsy showed normal architecture.

The child was rehospitalized twice during the ensuing three months because he continued to pass dark stools which were guaiac-positive, had a severe anemia, and had a recurrence of his ascites. Transfusions and diuretics were administered, with temporary improvement at each admission.

His fourth admission was on Sept. 5, 1953 (three months after his splenectomy), at which time an esophagoscopy was carried out by Dr. Trent Smith which revealed many large blood-covered varices at the esophagogastric junction. Three days later, after several transfusions, the child's abdomen was reexplored with the intent of establishing a portacaval shunt. The periumbilical and peritoneal ves-

sels along the right colic mesentery were tortuous and tremendously dilated. Attempts at dissection in the region of the porta hepatis proved fruitless because of bleeding from nests of collateral venous channels. The colon was retracted upward and the jejunum toward the left. A T-shaped incision was made into the base of the jejunal mesentery, and, after dissection through the hemorrhagic and edematous mesentery, the junction of the right colic and superior mesenteric vein was exposed. The latter vessel was 6 mm. in diameter and widely separated from the inferior vena cava by the interposed mass of edematous retroperitoneal tissue. To bridge this gap, we elected to use the transected, turned-up proximal end of the inferior vena cava.



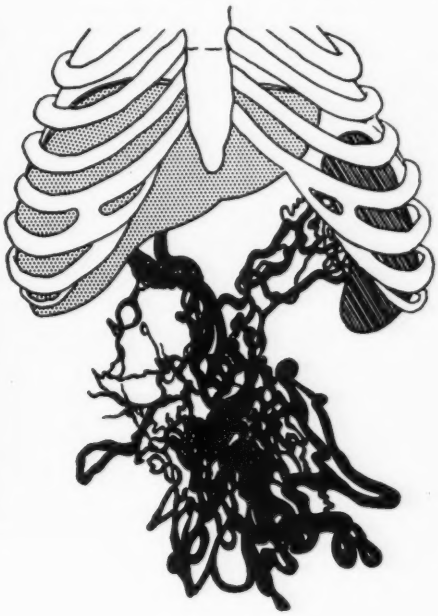


Fig. 4.—The portal venogram and artist's tracing of the portal vein pattern in a five-month-old infant with extrahepatic obstruction similar to Case 1.

The right colon and duodenum were displaced medially, and the inferior vena cava, between the origin of the renal veins and the confluence of the common iliac, was mobilized. This provided a segment of vena cava approximately 7 cm. in length and 2 cm. in diameter. A bulldog clamp was placed just below the junction of the renal veins. The inferior vena cava was transfixed and ligated and the vessel transected just above its origin. This free end was then passed through a tunnel in the retroperitoneal tissue inferior to the duodenum and up to the posterolateral aspect of the superior mesenteric vein. Additional bulldog clamps were then applied to the superior mesenteric vein, and side-to-end anastomosis between this vessel and the divided proximal end of the inferior vena cava was carried out with an everting running 00000 nonabsorbable surgical (silk) Deknatel suture. The anastomosis was completed in 23 minutes, and there was no undue congestion of the bowel due to temporary occlusion of the superior mesenteric vein. Upon removal of the clamps, there was no torsion at the suture line and a good surge of blood was seen to pass into the vena cava. The area was not retroperitonealized. The abdomen was closed in layers. The total blood loss during the six hour operation was 425 cc.

Postoperatively, the patient was mildly febrile for two days. The ascites did not recur, and there was no further bleeding. At no time was there evidence of venous insufficiency in the lower extremities. He was discharged home on the eighth postoperative day.

The child had two subsequent admissions to the hospital the following month owing to fever, diarrhea, recurrence of the ascites, and occult blood in the stools, associated with anemia. Each occasion he was given diuretics and a salt-poor diet and discharged in two or three days without transfusion. It was feared that his shunt had thrombosed. However, his subsequent course was much improved until March, 1954 (six months after the shunt procedure) when without provocation he experienced his second single episode of hemat-

emesis, which was treated by Dr. Glasscoch, of Ponca City, Okla., by the administration of 500 cc. of whole blood.

The patient was readmitted to The Columbus Children's Hospital on Sept. 15, 1954 (one year after his shunt), at which time his abdomen was relaxed but contained no fluid. The epigastric and lumbar veins were visibly dilated above and below his abdominal scar. The laboratory studies revealed the hemoglobin to be 11 gm., white-blood-cell count 11,300, normal differential and platelets, stools guaiac-negative, plasma prothrombin 100%, total protein 7.2 gm. per 100 cc. (albumin 4.1 gm. and globulin 3.1 gm.), thymol turbidity 10.1, and cephalin flocculation 0. Electrophoretic studies of serum gave the following results: gamma globulin 20.3%, beta globulin 11.8%, alpha globulin 12.25%, alpha$_2$ globulin 8.48%, and albumin 46.3%. Cholinesterase activity was 0.77 pH unit per hour, with normal values of 0.62 unit to 1.26 units. Recent reports from Dr. Glasscoch, in January, 1954 (eighteen months after the shunt), indicate that the child has had no further bleeding episodes and has been growing normally. The hemoglobin value is 13.7 gm. per 100 cc.; red-blood-cell count is 4,270,000, and his stools have continued to be guaiac negative.

Case 2.—The patient, a girl, was born on March 1, 1939, after a normal gestation and delivery. Shortly after birth, an infection of the umbilicus developed, which lasted about two weeks and was not associated with any generalized symptoms of toxicity.

Subsequently, this girl was considered normal throughout infancy and childhood and was first admitted to The Columbus Children's Hospital on Jan. 18, 1951, at the age of 12 years because of vomiting of clotted blood. At that time the hemoglobin was 11.3 gm. per 100 cc.; the red-blood-cell count was 3,300,000, the white-blood-cell count was 6600, and platelets were 30,150; prothrombin was 100% of normal; stool guaiac tests were persistently positive. The patient's symptoms subsided on conservative management, and she was discharged home.

She remained essentially well until Sept. 1, 1951 (nine months later), when she was readmitted because of a second episode of massive hematemesis. The hemoglobin was 11.2 gm. per 100 cc.; cephalin flocculation was 1+; thymol turbidity was

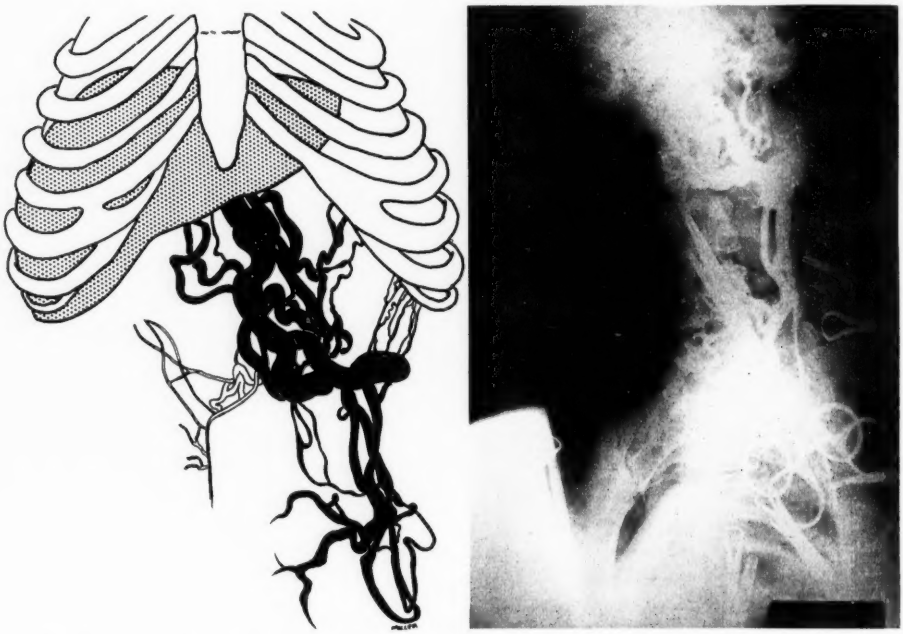


Fig. 5.—A portal venogram and the artist's tracing of the postsplenectomy portal vein bed in a 15-year-old girl (Case 2) with repeated episodes of massive hematemesis. Surgical treatment by anastomosis of the divided proximal vena cava to the "venous lake" in the base of the mesentery (indicated by arrows).

2.3 units; total protein was 7.3 gm., and prothrombin was normal. Radiologic studies, including an intravenous urogram and an upper gastrointestinal series, revealed no evidence of esophageal varices. The spleen was enlarged.

It was felt that the child was suffering from portal hypertension with secondary hypersplenism. On Sept. 14, 1951, she was explored through a left thoracoabdominal incision. A splenorenal shunt was anticipated. The portal pressure was 380 mm. of saline, and there were many evidences of collateral circulation and some edema of the bowel wall and the base of the mesentery. The spleen and tail of the pancreas were mobilized. The splenic vein was replaced by multiple small vessels apparently the result of thrombosis with recanalization. A splenorenal shunt was, therefore, impossible and splenectomy was performed.

After this procedure, the portal pressure fell to 180 mm. of saline, encouraging us to believe that perhaps this child had had a thrombosis involving only her splenic vein. Recovery from this operation was uneventful, and she was discharged home on the seventh postoperative day.

She remained well for 13 months, after which time she was readmitted, on Nov. 7, 1953, because of massive hematemesis. Hemoglobin was 6.7 gm. per 100 cc. Repeat upper gastrointestinal roentgenographic studies showed evidence of severe hypertrophic gastritis, but no esophageal varices could be demonstrated. She was placed on a medical regimen for gastritis and discharged to the care of her family physician, Dr. J. W. Hurt.

During the next four months, she experienced four episodes of hematemesis and was readmitted as a postsplenectomy bleeder on March 8, 1954, for a right-sided exploration. At this time her hemoglobin was 9.2 gm., her red-blood-cell count was 3,840,000; her white-blood-cell and differential counts were normal, her platelets were 230,000, and her stool was strongly guaiac-positive. A sulfobromophthalein test showed 19% dye retention in 30 minutes; the van den Bergh result was 0.55 mg., serum protein was 6.2 gm. (albumin 4.2 gm., and globulin 2.0 gm.); cephalin flocculation was 0, and thymol turbidity was 0.4 unit.

After repeated transfusions, the child was explored through a long right paramedian incision. There was a marked increase in vascularity of the abdominal wall. The small intestine was thickened and cyanotic. The mesentery and retroperitoneal structures were markedly thickened by edema.

A polyethylene cannula was threaded into a venous arcade in the midileal portion of the small bowel. The portal pressure was 310 mm. of saline, and 50 cc. of 70% sodium acetrizoate was injected. A single portal venogram was obtained (Fig. 5), which showed the portal vein to be replaced or recanalized by multiple tortuous vascular channels. The coronary vein and esophagogastric plexus were hugely dilated. In the region normally occupied by the superior mesenteric vein was a sizable venous lake. This was chosen as the site for a decompressive anastomosis and was dissected out with difficulty.

The right colon and duodenum were then mobilized toward the left. This entailed division of multiple collateral channels in the lateral mesentery and the retroperitoneal area. As the large lumbar vessels were individually ligated and divided, a segment of vena cava approximately 9 cm. in length was dissected free. Proximally, the vena cava was occluded with a Potts clamp placed just below the renal veins. Distally, it was doubly transfixed, ligated, and transected at the confluence of the common iliac veins. The proximal cut end was then passed through the retroperitoneal tissues and anastomosed to the side of the large portal venous channel, with everting Deknatel black 00000 nonabsorbable surgical (silk) sutures. The anastomosis was 2.5 cm. in diameter, and, following removal of the clamps, there was a grati-

Fig. 6.—Case 2. A 16-year-old girl with extrahepatic portal obstruction, one year after the ligation of the inferior vena cava and the performance of a side-to-end anastomosis between the superior mesenteric vein and the proximal end of the inferior vena cava. (Note normal lower extremities.)

fying visible drop in the portal pressure. The anastomosis functioned well but was somewhat angulated because of its necessary impingement on the very thickened edematous retroperitoneal tissues. After biopsy of the liver, the abdomen was closed and the patient was returned to the recovery room, having lost 1200 cc. of whole blood during the 10 hour procedure.

The postoperative course was complicated by thrombophlebitis involving the right saphenous vein, which completely cleared in two weeks prior to discharge from the hospital. The liver biopsy showed normal architecture. There has been no swelling of the lower extremities since that time, although the patient plays tennis, swims, and participates in all high school activities (Fig. 6).

There has been no recurrence of the gastrointestinal bleeding. Her most recent blood studies were red blood cell count 4,520,000, hemoglobin 12.5 gm. per 100 cc., white blood cell count 13,500, platelets 461,000. Fluoroscopic examinations of the esophagus showed no varices.

COMMENT

The clinical syndrome of anemia, gastrointestinal hemorrhage, ascites, and congestive hypersplenism have long been associated with abnormalities of the portal circulation. The gross pathologic features of this syndrome have been recognized for many years. Unfortunately, the effective management of the mechanical problem was delayed until the significance of the hemodynamics of the response of the portal venous system to obstruction was appreciated. Modern surgeons owe much to such men as Whipple, Blakemore, Rousselot, Linton, and Child, who not only realistically emphasized the importance of the "hypertensive factor" in portal obstruction but also were responsible for the development of effective surgical procedures for alleviating this pathologic state. Today, as a result of their enterprise, surgical decompression of the portal venous system is the accepted therapy in all suitable symptomatic cases of extrahepatic obstruction and, in most clinics, of intrahepatic obstruction as well.‡

Patients with intrahepatic portal-vein obstruction due to primary liver disease and cirrhosis are currently treated by a splenectomy and an end-to-side splenorenal venous shunt or a portacaval shunt. Such desirable shunts may be technically impossible because of distorted anatomy or uncontrollable bleeding from collateral vessels of the periportal or perisplenic areas.

Patients with extrahepatic venous obstruction present a more difficult problem. Localized extrahepatic obstructions are relatively uncommon. Intrinsic stenosis or atresia,[14] localized valves,[15] and the occasional extravascular compression syndromes due to neoplasm or inflammation [16] have been described and should be searched for in every case because they may represent relatively simple types of extrahepatic obstructions to deal with surgically. However, the majority of extrahepatic blocks to portal venous return flow are the result of a congenital or acquired episode of thrombosis or thrombophlebitis of the portal vein and/or its tributaries. The anatomical derangement that results depends not only upon the extent of the original thrombotic process but also upon the effectiveness of the collateral circulation which develops subsequently. Isolated thrombotic processes may occur and if present in the splenic vein alone may best explain why in certain rare instances permanent long-term relief from hemorrhage from esophageal varices has followed such simple surgical procedures as splenectomy alone.

Fortunately, with the use of portal venography at the time of operation, it is possible to establish with certainty the exact configuration of the extrahepatic portal circulation. This simple adjunctive procedure can make excruciatingly clear the anatomical vascular problem with which the surgeon must deal. Occasionally, neither the splenic nor the portal vein is of sufficient size to warrant an attempt at splenorenal or portacaval anastomosis. In such instances one may demonstrate a sizable tributary or collateral vessel, such as the superior or inferior mesenteric vein, lying deep in the substance of the mesentery or a venous lake formed by the confluence of several collateral venous tributaries, which can be utilized for decompressive purposes. Anastomoses between such

‡ References 1, 11, 12, and 13.

lesser vessels as the inferior mesenteric vein or branches of the superior mesenteric vein and the renal or ovarian vein have been accomplished with uncertain results because of the small size of the anastomotic vessels and because frequently only one end of the portal vessel can be utilized.§

Rousselot has successfully circumvented this obvious difficulty in several instances in adults by using autogenous venous grafts as a bridge between the inferior vena cava and the dilated portal venous vessels or lakes, with good results.[10] When a suitable donor vein is readily available, such a procedure has much to recommend it.

The anastomosis between the side of the superior mesenteric vein and the end of the inferior vena cava, which we have used in the experimental animals and in two patients, is hemodynamically similar to the vein-graft technique. Both provide a long venous channel vein which can be utilized to bridge the gap between the inferior vena cava and the dilated portal venous radicle. We have found that the turned-up inferior vena cava provides a shunt with a large orifice and but a single anastomosis into which the venous drainage from all segments of the portal system can flow directly into the systemic venous stream. The liver is not completely bypassed by portal blood by such a procedure, a fact which also may be of theoretical advantage.[17]

This shunt offers certain advantages over the autogenous vein-graft technique: (1) a single anastomosis, (2) a larger anatomic orifice, and (3) a technique useful in children where available donor veins for grafting are small. The disadvantage of this method is that the systemic blood returning from the lower extremities and pelvis will, of necessity, have to pass through and develop collateral channels in the inferior epigastric, ileolumbar, internal vertebral, and lumbar vessels. However, the elective ligation of the inferior vena cava has, in the absence of preexisting thrombotic disease, been well tolerated.

§ References 1 and 8.

SUMMARY

Experimental and limited clinical experiences with a previously unreported side-to-end type of portal-to-systemic venous shunt, designed primarily for those patients in whom the splenic and portal vein sites are unavailable for decompressive procedures, have been presented.

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DISCUSSION

On Papers by Drs. William A. Altemeier and William T. McElhinney; George A. Hallenbeck and Everett Shocket, and H. William Clatworthy Jr., Thomas Wall, and Robert N. Watman

Dr. Jacob K. Berman, Indianapolis: This discussion on portal hypertension indicates the widespread interest in this enigmatic disease. The ingenious ways of producing venous shunts as described by Drs. Hallenbeck and Schocket in extrahepatic blocks and by Drs. Clatworthy, Wall, and Watman in both extra- and intrahepatic obstruction is evidence that many researchers are continually seeking to ameliorate the vascular crises in portal obstruction. Drs. Altemeier and McElhinney have asked me to discuss their paper, and, therefore, I shall confine my remarks to their summary of the treatment of portal hypertension with hepatic arterial ligation.

The contraindications for the use of this method are, in general, those which we have previously stipulated: Hepatic arterial ligation should not be used in the extremely large postnecrotic liver or in patients who are actively bleeding or in those with deep jaundice. In fact, we have repeatedly warned that if the method is to be properly evaluated it should be used only in advanced atrophic cirrhosis. Many of our observations have been confirmed by Drs. Altemeier and McElhinney. These include the immediate fall in portal pressure after hepatic ligation, an additional fall after splenic arterial ligation, a sustained fall for over three years in at least one of their cases, the unpredictable results by our earlier methods of ligation, the improvement in liver profile in those who recover, and the potentially excellent results in those who survive more than five months. Their mortality rate is high, and this, as previously reported, was our experience with our earlier methods of ligation.

The authors have performed a valuable service in their studies on devascularization of the liver. In fact, their cases are the only ones that I know of in which hepatic arterial ligation was followed by portacaval or splenorenal shunt as a staged procedure.

Devascularization of the liver is followed by death in four days according to Child. Madden attempted to ligate the superior mesenteric vein and the patient died, apparently of mesenteric thrombosis. The experimental work with devascularization by Rappaport and his associates, by Popper and his group, and by us indicates that immediate ligation of both hepatic arterial and portal venous inflow is followed by death in 100% of cases. However, this can be done as a graded procedure with survival, but all animals ultimately die with a syndrome that is not unlike that of hepatic failure in progressive atrophic cirrhosis. Apparently animals as well as patients in these cases live on a borrowed circulation.

Portal pressure is a symptom and not a disease. It indicates that the hepatic venous outflow is curtailed. In one of our early publications (A. M. A. Arch. Surg. **63:**379, 1951) we stated that "free exit of blood from the portal sinusoids into the central vein is delimited." In a paper scheduled for publication in the April issue of the *Journal of Digestive Diseases* we have tried to outline some of the causes for the increase in hepatic venous pressure. These may be categorically outlined as follows:

1. The Bernoulli principle is a factor. The conversion of kinetic energy into potential energy in a narrowed vascular tree which becomes divergent after the point of occlusion gives rise to increased hepatic venous pressure.

2. There is an angiomatous transformation of the liver, as we have previously stated. Knisely has clearly shown that there are hepatic artery shunts as well as hepatic vein and portal-hepatic vein shunts.

3. The increase in hepatic venous pressure is probably due in greatest measure to perivenous fibrosis.

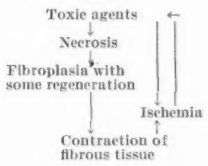
4. There is no reservoir function left in the liver, and therefore the hepatic vein pressure is more likely to be increased.

Communications between the hepatic artery and the portal vein are more intimately associated, and this is reflected in the increase in sinusoidal pressure and, consequently, in accordance with our hypothesis, in the hepatic venous pressure as well owing to the Bernoulli principle.

6. There is an increase in total blood volume, which is probably due in part to the "parasitic circulation" within the liver itself.

Fibrosis of the liver is the key mechanism causing the vascular crisis and ultimately hepatic failure. It is very much like silicosis in the lungs and

continuous long after the causative agent has been discontinued. Dr. Adams told me yesterday that he had recently seen a case in which pulmonary silicosis was accompanied by hepatic silicosis and also by pancreatic silicosis. The scarred liver in atrophic cirrhosis results from toxic agents, such as alcohol, virus infections, bacteria, and poisons; but once the blood supply is greatly curtailed and ischemia itself prevents proper oxygenation of the liver cell and produces necrosis and fibrosis. In this regard a vicious circle is established which may be outlined as follows:



The treatment of atrophic cirrhosis is twofold—the relief of the vascular crisis and the interdiction of the progressive fibrosis. The former may be temporarily relieved by portal-systemic shunts or by hepatic artery occlusion. In our earlier work we ligated close to the celiac axis but found that collateral circulations soon took over and that, what is more important, we had overlooked substitutionary and accessory arteries to the liver. We also found that ligation close to the liver was inevitably followed by death in the experimental animal and was dangerous in man; so we could not use this approach. Therefore, we are now slowly occluding the hepatic artery inflow and its additive or substitutional vessels, by methods which we have previously described. Portal-hepatic circulation may be improved by this procedure because it stops the competition between the portal vein and hepatic artery inflow. Gradual occlusion invites collateral blood supply, so that ischemia may be relieved and regeneration rather than necrosis may ensue.

Our attention must also be directed to the arrestment of fibrosis. This may be prevented by discovering the causes of the disease and eliminating them. After progressive fibrosis is in action, dietary measures and drugs, such as corticotropin, cortisone, and thyroid extract, may be tried, based upon the fact that they may inhibit fibrinolysin or stimulate the production of antifibrinolysin, which delimits fibroplasia.

We are now using antihistamine drugs in doses of 200 to 300 mg. a day to inhibit fibroplasia. This treatment is based upon the experimental work which we published in the *American Surgeon* (Vol. 19, No. 12, 1953). Antihistamines were noted by Kohlstaedt to be fibroblastic inhibitors, while producing systemic hypertension in dogs. He wrapped the kidney in a silk envelope dusted with sulfathiazole, after the method of Page, and noted the inhibition of fibroplasia by thenylpyramine (Histadyl).

I was very much interested in Dr. Holden's findings of portal vein contamination from the bowel. I believe we should prepare our patients with intestinal antibiotics and chemotherapeutic agents such as neomycin and phthalylsulfathiazole (Sulfathalidine) in an effort to sterilize the gastrointestinal tract prior to hepatic surgery.

Dr. John T. Reynolds, Chicago: I believe we all would like to encourage Dr. Berman to promote regeneration of the liver, and everyone will anticipate the moment this occurs. However, in the meantime we do have technical problems, and I believe two things everyone who is operating on these cases must keep in mind are these: first, the poor risks; second, the patients who are very difficult to operate on. It is not always easy, as indicated, simply to tie the hepatic artery or to isolate the splenic vein, and so we welcome such suggestions as Dr. Hallenbeck's. This suggestion may allow us to decide what sort of operation these patients should have. We can thus possibly avoid the unpleasant experience of encountering a thrombosed splenic vein.

Just as Dr. Rousselot's addition of splenic venograms is a great help, so this visualization of the superior mesenteric vein by direct cannulization should allow us to decide whether we should proceed.

On the question of venous pressures, I have had two experiences that were significant. Dr. Julian had a patient in whom the vena cava was obviously under much more pressure than the pressure present in the portal vein, and for this reason an anastomosis was not done but an esophagectomy was done. Autopsy revealed the fact that the patient had a congenital stricture of the vena cava.

I have had another patient in whom the portal pressure was lower than the pressure of the vena cava. There seemed to be no other reason not to proceed with the anastomosis, and at the conclusion of the anastomosis the blood was seen rushing very vigorously from the portal vein into the vena cava. I believe that the low portal pressure was obtained because we did not take the pressure as soon as the portal vein in any branch was exposed. While the dissection was being done, we lost blood from the portal system and this was sufficiently voluminous that the venous pressure did not reflect the condition of the portal pressure in an undisturbed preparation.

If we are going to depend upon these pressures, I believe they should be taken very early in the dissection.

Dr. William J. Potts, Chicago: There is much confusion and uncertainty about the whole subject

of portal hypertension in diseases of the liver in children. We have departed from the accepted procedures in a couple of cases which I would like to present briefly.

[Slide] This child was 20 months old four years ago and weighed 13 lb. Its albumin-globulin ratio was reversed, the liver function tests showed signs of failure and the child was jaundiced and had a huge abdomen. We removed about 1 liter of fluid each week by paracentesis.

The pediatrician rather strongly urged a shunt operation. The surgical department felt this was the wrong thing to do because of the jaundice and the fact that the child had never bled. However, with nothing else to offer, we finally agreed to a portacaval anastomosis. The opening was made almost 2 cm. in diameter. Following operation, the child improved markedly and in a year more than doubled in weight. Further tapping was unnecessary. The child developed pneumonia and rather suddenly died. At postmortem examination we found the anastomotic channel 1.5 cm. in diameter between the portal vein and the inferior vena cava open and free from surrounding clots. The liver showed signs of advanced cirrhosis. The shunt seemingly was influential in relieving the severe ascites.

[Slide] The second case was still a greater problem. This child, 13 months old, weighed only 9 lb. Its abdomen was tremendously distended with ascitic fluid. Liver function tests and protein levels were normal. We made an incision on the right in anticipation of performing a portacaval shunt but could do nothing because the portal vein was a mass of irregular small veins.

The parents were most cooperative and agreed to a second operation on the left, with the faint hope that we could do a splenorenal shunt. At operation, we found not one spleen but a number of little nubbins of spleen, like a hill of potatoes. There was nothing to do but remove all these little spleens.

[Slide] This slide shows the child six months later. You see he is healthy and well nourished. Ascites has not recurred, and the child has continued to thrive three years after surgery. Why?

There are still many unknowns in the matter of liver disease and portal hypertension in children. The suggestion made this morning by Dr. Clatworthy certainly has much merit and may be of value in unusual cases.

DR. ROBERT E. L. BERRY, Ann Arbor, Mich.: This frank discussion is indeed refreshing. We first started doing splenorenal shunts but abandoned the operation because we felt we could get a better and larger anastomosis by using the portal vein and the inferior vena cava. Furthermore, the removal of the spleen may destroy a vascular collateral circulation that these individuals may subsequently need.

I would like to point out that in recent operations we have been using hypotensive anesthesia. At first it seemed a paradox to use such anesthesia in the presence of a badly damaged liver, but our experiences have shown that it is a safe procedure.

Not only may the operating time be reduced by about 50%, but the amount of blood that has to be transfused during the operation can be reduced by approximately the same percentage.

We have had no reasons to regret the use of hypotensive anesthesia and have maintained these patients for as long as three hours at a brachial artery systolic blood pressure of 65 to 70 mm. of mercury.

DR. WILLIAM A. ALTEMEIER, Cincinnati: We certainly do not wish to give anyone the impression that we are recommending the procedure of hepatic and splenic artery ligation at the present time for the treatment of cirrhotic patients with portal hypertension. This study represented a series of 18 cases which we have operated on and on which we are collecting data.

In general, the results that we have obtained with hepatic artery ligation have been inferior to those obtained with the shunts, and our best results have been with splenorenal anastomoses. Every one of these patients is living at the present time. There has been an incidence of recurring hemorrhage in a little less than one-third of the cases.

The over-all mortality of 50% during the three and one-half year period in the series of hepatic artery ligations is considerably higher than the over-all mortality of 23% which we obtained in the shunt cases.

There is some question in our mind as to whether the interruption of the portal blood flow by an end-to-side portacaval shunt is followed in some cases by progressive and more rapid liver damage than that which occurs after a splenorenal anastomosis.

There are several things I should like to leave with you in regard to the patients who have undergone hepatic artery ligation. The recurrence of bleeding seemed to have some definite relationship to the size of the spleen. In those instances in which the spleen shrank in size and became nonpalpable, recurrent bleeding was absent. However, if the spleen again became enlarged and palpable, gastrointestinal hemorrhage was the result.

In one of the cases the pressure in the portal system was normal at the time of the portacaval anastomosis, done approximately 28 months after the original hepatic and splenic artery ligation. In another case it is interesting to note that the hepatic artery had become thrombosed up into the

hilum of the liver. In a third patient, weak pulsations were noted to have recurred and to be present 30 months after hepatic artery ligation, suggesting that collateral circulation had developed. The spleen then became enlarged and recurrent hemorrhages had developed.

The postnecrotic cirrhosis cases have been of particular interest to us in that these have been associated with a very high mortality when subjected to hepatic artery ligation. I personally consider this condition a contraindication to the operation.

A note of warning concerns the friability of veins in patients with cirrhosis and ascites. These veins will rupture spontaneously during mobilization of the spleen or in an attempt to dissect the splenic vein. The walls are waterlogged and extremely friable. This applies both to cases of hepatic artery ligation and to portacaval or splenorenal shunts. We cannot emphasize too much the necessity of "wringing out" these patients to get rid of their ascites beforehand.

To conclude and to bring to you our present thoughts on this matter, I would like to cite a case which I saw last week in consultation with a physician who had previously referred a patient on whom we had done hepatic and splenic artery ligation three and one-half years ago. This latter patient has done so well that the referring doctor requested that we do hepatic and splenic arterial ligations on this new patient.

I spent an hour and a half convincing him that I would prefer to do a splenorenal shunt on this particular patient.

The Source of Fat in Fat Embolism

W. W. GLAS, M.D., Eloise, Mich.
M. M. MUSSELMAN, M.D.
and
H. L. DAVIS, Ph.D., Omaha

Despite the hundreds of articles written on the subject of fat embolism since the seventeenth century, there is a great discrepancy of opinion as to its clinical importance, methods of diagnosis, etiology, and treatment.

We believe that fat embolism is common in persons suffering from injuries and that the effects may be serious. We studied 109 patients consecutively admitted to the hospital for injuries. Half of them had fat embolism as diagnosed by the finding of fat in the urine, and 10% of the severely injured died from the effects of fat embolism.[1]

Treatment of this disease has been nonspecific and supportive. If we are to develop better treatment we must learn more of its etiology. In these experiments we have concerned ourselves with the origin of the fat.

Three possibilities for the origin of the fat have been suggested.

1. Mechanical. Fat liberated at the site of trauma gains access to open veins. This concept has been the most popular and is supported by numerous reports of bone marrow embolization. However, Lehman injected cottonseed oil into dogs as a substitute for bone marrow fat and calculated that there was insufficient fat in a human femur to produce fatal fat embolism.[2]

2. Humoral. This second concept is that chylomicrons and other formed elements of the blood are mutually repellent and stabilized in suspension by a negative charge. This charge results from bound protein and water on the chylomicron. The stability may be broken either by neutralization of the charge or by dehydration. It is possible that stress may release cations, such as calcium and magnesium, or histamine which neutralizes the charge, or stress may mobilize lipids which displace bound water.

3. Trigger. The third concept is that the entrance of a small amount of fat into the veins is the trigger which breaks the physiological fat emulsion. If true, fat emboli are composed mainly of fat from the blood rather than fat from the tissues.

METHODS

This study was carried out to evaluate the concepts listed above. Bone marrow fat was removed from the femur of a rabbit and injected intravenously into another rabbit to determine if there was enough fat in a femur to cause death.

To determine how soon fat embolism occurred after injury, both femurs were fractured in rabbits. The animals were killed immediately with a crushing blow to the head.

The adrenals were removed before the femurs were fractured in another group of animals to determine the role of the adrenal glands.

Massive doses of corticotropine (ACTH) and cortisone* (Table 4) were given to rabbits to evaluate their effect with regard to initiating fat embolism.

It has been suggested that shock may initiate or aggravate fat embolism. To determine if hemorrhagic shock aggravated traumatic fat embolism,

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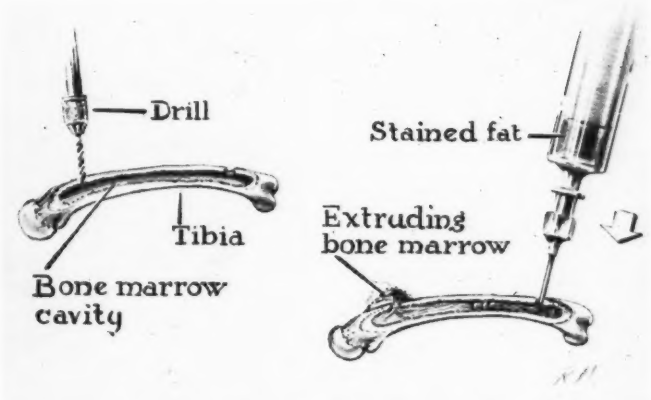

Fig. 1.—Method for introducing stained fat into marrow of rabbit before fracturing femur. After fracture, stained fat could be seen in lung grossly (Fig. 2).

rabbits were subjected to hemorrhagic shock, after which both femurs were fractured.

To determine how much fat was mobilized from the marrow after fracture, stained fat was injected into the tibial bone marrow cavity of control rabbits and others followed by fracture. Figure 1 illustrates the techniques used.

In order to compare the results from these various experiments, a microscopic grading system for fat embolism was devised. The lungs were selected for study because they are the most frequently involved of all organs (Table 1).

TABLE 1.—*Grading of Fat Embolism: Microscopic Examination of Lung*

0—No emboli in entire section (about 1 square cm.)
1—One to four emboli in entire section
2—Five to ten emboli in entire section
3—Emboli in each low power field
4—Many emboli in each low power field

RESULTS

Intravenous injection of the femoral bone marrow fat resulted in death in 9 out of 10 cases. In an average rabbit of 3.5 kg. this is approximately 2.0 cc. of bone marrow fat which was given in a period of 10 minutes. Injection of an equal amount of corn oil resulted in no deaths (Table 2). This is well below the lethal level as determined by Scuderi in experimental work on dogs.[3]

Twenty-four hours after fracture of both femurs an average microscopic Grade 3 fat embolism was found. This represents severe fat embolism (Table 3). In animals killed immediately after fracture of both femurs a 2+ grading of fat embolism was found.

TABLE 2.—*Source of Fat in Fat Embolism in Rabbits: Bone Marrow Fat and Corn Oil U. S. P.*

Bone Marrow Fat from Femur Injected Intravenously (2.0 Cc. Fat)	
No. of Rabbits	Mortality
10	9
Corn Oil 2.0 Cc. Injected Intravenously	
10	0

Removal of the adrenals did not prevent fat embolism, as shown by the finding of Grade 2 fat embolism after fracture of the femurs (Table 3).

Table 4 shows the results from the administration of cortisone and corticotropin. The controls had a higher grade of fat embolism than did the hormone-treated animals. We found a fat cell embolus in one animal treated

TABLE 3.—*Source of Fat in Fat Embolism in Rabbits: Fractures*

Procedure	Average Grade of Microscopic Fat Embolism
Fracture of both femurs (24 to 48 hr.)	3
Fracture of both femurs, head crushed immediately	2+
Femoral fractures after bilateral adrenalectomy	2

TABLE 4.—*Source of Fat in Fat Embolism in Rabbits: Cortisone and Corticotropin*

Procedure	Average Grade of Microscopic Fat Embolism
Cortisone, 120-600 mg./kg. in 12 hr.	1+*
Corticotropin, 120-600 units/kg. in 12 hr.	1—
Control—normal saline, 15 cc. in 12 hr.	2

* In one instance there was microscopic evidence of fat-cell embolization.

with cortisone. Only mechanical injury of fatty tissue with liberation of the cell at the site of trauma could explain the presence of this cell in an arteriole of the lung. Since the only injury in this case was the injection of cortisone, the cell must have been dislodged by this process. None of these groups revealed as much fat embolism as when the femurs were fractured.

Contrary to expectation, if the humoral theory applies, preexisting hemorrhagic shock reduced the amount of fat embolism found in lungs after fractures. Table 5 refers to the effect of hemorrhagic shock.

Large amounts of stained fat appeared in the lungs after injection of the stained fat

TABLE 5.—*Fat Embolism in Rabbits*

Procedure	Average Grade of Microscopic Fat Embolism
Femoral fractures (control)	3
Femoral fractures after hemorrhagic shock	1

into the marrow cavity followed by fracture (Fig. 2). Green-stained fat globules were easily seen on microscopic examination of a frozen section. When a fat with a low melting point was used, such as corn oil, more fat embolism occurred than when a fat with a higher melting point, such as hydrogenated cottonseed oil (Crisco), was used. Hydrogenated cottonseed oil was used because it closely resembles human bone marrow fat with regard to its melting point and viscosity. Table 6 shows the microscopic grading of the lungs with the two different fats. The controls showed a moderate amount of fat embolism, demonstrating the vascularity of the marrow cavities. It appears that the physical properties of the fat are an important factor in fat embolism.

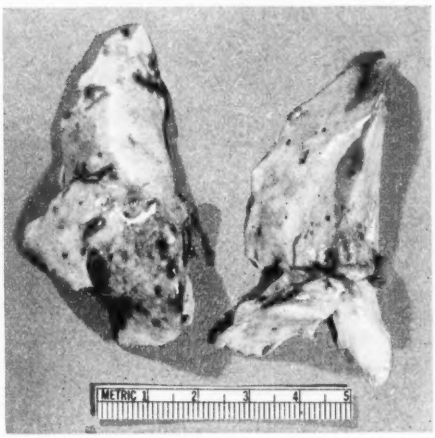

Fig. 2.—Lungs of a rabbit 48 hours after injection of green-stained fat into the tibial bone marrow cavity and 24 hours after fracture. Green fat shows on surface of lungs here as light gray mottled areas.

COMMENT

Lehman's conclusion that there is not enough fat in the femur of a man to kill him has often been quoted. If this is true, where does the fat which causes death from fat embolism come from? We have approached the question raised by Lehman directly by injecting the fat from the marrow of the femur of one rabbit into the veins of another. Eight of ten rabbits in which this was done died. That there was sufficient fat in the femur of one animal to kill another one of the same kind and size suggests that there is enough fat in the marrow of the femur of an animal to kill it.

Fat embolism occurred within seconds after the fracture of both femurs. It is

TABLE 6.—*Difference Between Fats*

Injection of Stained Fat into Marrow Cavity of Tibia	Average Microscopic Grading	
	Corn Oil	Hydrogenated Cottonseed Oil
Fracture	4+	3+
No fracture (control)	2+	2

difficult to believe that a physiologic response to stress could have been responsible for this fat embolism, because humoral mechanisms act more slowly. Fat embolism was produced by fracturing femurs even in the absence of the adrenals. It would appear that the function of intact adrenals is not a necessary part of fat embolism. We were unable to produce significant fat embolism by giving massive doses of corticotropin and cortisone in an effort to simulate a stress reaction. These results fail to support the stress, or humoral, theory for the etiology of fat embolism.

The existence of hemorrhagic shock before fat embolism was caused by fracturing the femurs of our animals subtracted from, rather than added to, the amount of fat embolism which was found. Possibly because of the impaired circulation, less fat was carried to the lungs.

Our procedure of introducing stained fat into tibias before we fractured them was admittedly unnatural. However, under these conditions, it was demonstrated grossly as well as microscopically that fat was transported from the marrow to lodge in the vessels of the lungs.

The amount of fat embolism observed in our animals varied with the physical properties of the fats producing the fat embolism. Less fat embolism occurred with fat having a high melting point. Less fat embolism occurred with hydrogenated cottonseed oil than with corn oil.

SUMMARY AND CONCLUSIONS

1. The fat in the marrow of the femur of one rabbit was sufficient to cause fatal fat embolism when injected intravenously into another rabbit of similar size.

2. Fat embolism occurred in seconds after fracture of the femurs.

3. Fat embolism occurred in the absence of the adrenals. Significant fat embolism did not occur from the administration of corticotropin or cortisone.

4. Less fat embolism was found in rabbits if their femurs were fractured while they were in hemorrhagic shock.

5. A significant amount of fat was transported from the marrow cavity of a fractured bone to the lungs. This was partially dependent upon the physical properties of the fat.

6. These results fail to support the humoral or trigger theories of fat embolism.

DISCUSSION

DR. LOUIS G. HERRMANN, Cincinnati: We have followed the work of Drs. Glas, Davis, and Musselman with great interest, since we, also, believe that fat embolism is a common and often serious complication of trauma to the human body.

The clinical diagnosis of fat embolism is often difficult to establish in patients who suffer from extensive trauma to various parts of the body and especially in those patients with concomitant serious injury to the skull and brain.

The fracture of long bones in wounds of violence may permit large quantities of fat to be sucked into the veins which are held open by the matrix of the bone. It is also possible to liberate large quantities of fat into the venous system by severe trauma to long bones without fracture of the cortex of the bone.

We have long been of the opinion that fat embolism was largely on a physical basis, but some of the recent chemical studies of Davis and Musselman made us feel that the problem should be reevaluated.

The alcohol-dextrose treatment of fat embolism, which we have advocated since 1933, has proved the most effective clinical means of changing the physical qualities of the fat so that it will pass through the capillary networks of the lungs, brain, and viscera without producing serious hypoxia of vital tissues. Originally we used a special mixture of seven parts of 25% glucose to three parts of 96% ethyl alcohol for the intravenous solution and gave it in quantity sufficient to provide an effective therapeutic dose of approximately 5 cc. of the mixture per kilogram of body weight.

Since 5% alcohol in 5% dextrose now is easily available as a commercially prepared solution for intravenous administration, we have used this latter product in quantities of 2 to 3 liters per day in all seriously injured patients in whom we suspect fat embolism. The alcohol in this quantity has a sedative effect without depressing the respiratory center and, therefore, can be used in patients with associated injury to the skull or brain. We believe that this method is the most effective means of overcoming the serious sequella of widespread fat embolism.

DR. J. DEWEY BISGARD, Omaha: I too have been very much interested in this subject. Because I

have carried out some studies in the past in relation to fat embolism. Dr. Musselman asked me if I would discuss his paper.

Clinically, the more surgeons and pathologists look for evidence of fat embolism, the oftener they find it. It probably occurs in the minor or subclinical degree in most if not all fractures and severe injuries. Its clinical importance is difficult to evaluate. It may be the sole cause of death in many cases of severe injury, but this can be questioned because in these cases, as Dr. Herrmann pointed out, there are other associated factors, such as hemorrhage, head injuries, atelectasis, and so on.

Several years ago Harris pointed out that diffuse pulmonary changes which had been interpreted as diffuse atelectasis and pneumonia often in reality were interstitial and alveolar hemorrhage resulting from fat occluding the capillaries. He also showed that there was often an abrupt drop in the red-blood-cell count, which he attributed to loss of blood in the lungs, and he felt that this drop in the red-blood-cell count was of some importance as a diagnostic sign.

A few years ago I carried out some experiments suggested by the possible solvent effect of ether in the blood and in the lungs during ether anesthesia. In the animals anesthetized with ether there was much less of the fat which had been injected intravenously in the lungs than in the controls, but there was more fat in the urine. From this it was concluded, as Dr. Herrmann has indicated again, that ether probably dilated the capillaries in the lungs, permitting the fat to pass this barrier.

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Investigations of Serum Protein Changes in Combat Casualties

The Systemic Response to Injury

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Previous studies in the disturbance of protein equilibrium following surgery and injury in man and experimental animals have shown a catabolic phase, or period of negative nitrogen balance, followed by an anabolic phase, or period of positive nitrogen balance.* The serum protein changes during the catabolic phase were described by Cuthbertson and Tompsett [4] primarily as a loss of albumin and an increase in globulin. However, the procedure used was a salt precipitation technique that did not separate the a_1 and a_2 globulin fractions from the albumin. More recently, Hoch-Ligeti, Irvine, and Sprinkle,[5] using paper-strip electrophoresis, studied the serum protein changes in a group of 45 surgical patients. Their results indicated a significant decrease in the albumin fraction and an increase in a_1 and a_2 globulin fractions in 80% of patients within four days following operation.

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* References 1, 2, and 3.

PURPOSE

The massive trauma and extensive surgical procedures experienced by combat casualties are relatively uncommon in civilian medical practice. A thorough understanding of the quantity as well as quality of the metabolic response is important for the advancement of the medical treatment of these patients. It is for this reason that these studies were undertaken. The specific purpose of this study was to investigate the serum protein changes following major trauma and surgery and to determine if a qualitative or quantitative difference in the response existed between various types of wounds.

METHODS

The changes in serum protein fractions were investigated in 33 combat casualties. All patients studied were young, male, United Nations combat casualties, sustaining injuries from artillery, mortar, grenade, land mine, or small arms fire. Some were critically injured, sometimes with imperceptible pulse and blood pressure at the time of admission. In general, they represent the types of casualty that required immediate resuscitation, including extensive surgical treatment.

Serial samples of venous blood were collected for serum from all patients beginning immediately after operation and continuing to the time of evacuation. Preoperative samples were drawn if plasma expanders or albumin had not been previously administered and if hemorrhage was under control. Many patients received dextran or modified fluid gelatin postoperatively. The protein studies herein reported are exclusive of the period when the serum contained more than 3 mg/ml. of the plasma expander, as evidenced by chemical analysis. This was necessitated by the interference of the expander with the fractionation procedure at concentrations above this level.

The procedure employed for protein fractionation was based on neutral salt flocculation, using 28% sodium sulfite—a procedure that give results most

TABLE 1.—*Total Protein Values and Albumin-Globulin Ratios for Thirty-Three Patients*

Patient	Wound Description	Time After Wound, Hr.	Total Protein, Gm./100 ml.	Albumin-Globulin Ratio
1	Abdominal: multiple perforations of small intestine, fracture of ileum	17	7.8	1.1
		65	7.0	0.8
		89	6.8	0.8
2	Abdominal-extremity: multiple perforations of small and large intestines, perforation of iliac vein and artery, of both buttocks, right forearm, and flank	11	7.7	1.1
		42	6.0	0.8
		66	7.3	0.6
		89	7.3	0.7
3	Abdominal-extremity: perforations of sigmoid colon, of superficial femoral arteries; fractures of sacrum, both tibia; fibula; innumerable soft-tissue wounds	28	6.7	1.2
		61	5.8	0.7
		85	5.4	0.7
4	Abdominal-extremity: perforations of abdomen, and extremities, transfusion reaction oliguric 24 hr. postoperative	55	5.1	0.9
		77	5.2	0.8
		101	5.7	0.8
		125	5.6	0.8
5	Abdominal: perforations of colon and injury to cauda equina, paralysis of both legs	24	6.0	1.3
		52	5.2	1.0
		76	5.4	1.0
		100	5.1	0.9
		124	5.1	0.8
		148	4.8	0.8
		172	4.6	0.8
		196	5.2	0.7
6	Abdominal-extremity: wounds of both legs, left thigh, scrotum, face; perforations of chest and large intestine	3	7.4	0.9
		11	7.5	0.9
		63	6.4	0.9
		91	6.8	1.0
7	Abdominal: perforations of ascending colon and liver; laceration of kidney	21	5.7	1.2
		26	6.4	1.1
		40	5.3	0.9
		64	5.8	1.0
		89	6.9	0.8
8	Abdominal: perforations of ileum and rectum, compound fracture of sacrum	41	5.7	1.0
		65	6.0	0.9
		89	5.8	0.9
9	Abdominal: gunshot wound perforations of the liver, kidney and colon; renal insufficiency postoperatively; died of renal abscesses	4	6.9	1.5
		12	8.3	1.0
		42	4.6	0.8
		66	4.6	1.3
		89	5.1	0.9
		113	5.8	1.0
		137	5.8	1.0
		163	6.2	0.9
10	Abdominal-extremity: perforations of intestine, penetrating wounds of both thighs and a fracture of right femur	12	6.3	1.5
		33	5.7	1.6
		45	5.7	1.5
		69	5.9	1.3
		93	6.1	1.3
		111	5.3	1.4
		141	5.5	1.0
		165	5.5	0.9
		189	5.8	0.9
11	Abdominal-extremity: perforations of ascending colon and right flank; compound fracture of right ileum	6	5.2	1.1
		21	4.7	1.3
		27	4.6	1.3
		43	4.9	1.1
		67	5.0	0.9
		91	5.1	0.8

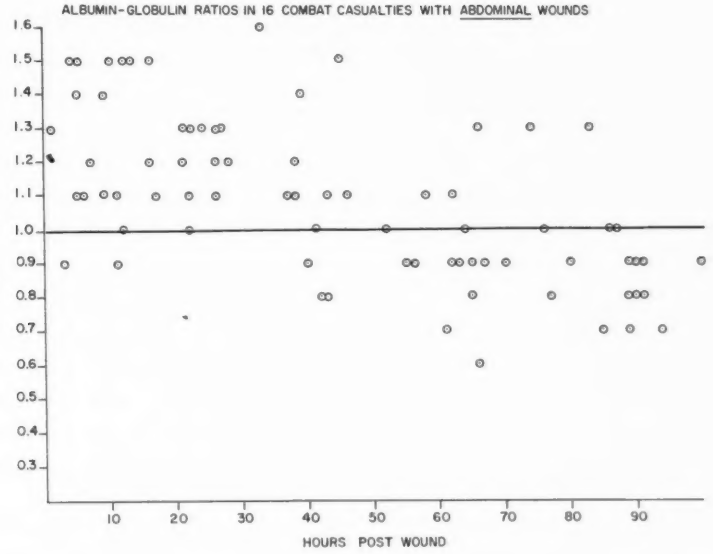
TABLE 1.—*Total Protein Values and Albumin-Globulin Ratios for Thirty-Three Patients*—Continued

Patient	Wound Description	Time After Wound, Hr.	Total Protein, Gm./100 ml.	Albumin-Globulin Ratio
12	Abdominal: lacerations of ileum and sigmoid colon, retroperitoneal hematoma; multiple soft tissue wounds of buttocks, hip, and back	9	7.1	1.4
		26	6.5	1.2
		38	6.5	1.2
		62	9.4	1.1
		86	6.2	1.0
13	Abdominal: perforations of intestine and spleen; splenectomy performed	5	7.4	1.1
		9	6.3	1.1
		16	6.9	1.2
		22	7.0	1.0
		32	7.0	1.1
		56	5.6	0.9
		80	5.6	0.9
14	Abdominal: perforations of intestine and bladder	1	7.1	1.3
		5	6.2	1.5
		13	6.3	1.5
		16	6.3	1.5
		22	6.9	1.3
		34	6.5	1.4
		58	6.5	1.1
		83	6.0	1.3
		107	6.6	1.2
		131	5.4	1.2
15	Abdominal-extremity: perforation of intestine and liver; penetrating wounds of right hip and leg	5	5.3	1.4
		7	5.6	1.2
		22	7.5	1.1
		46	5.7	1.1
		70	6.9	0.9
		94	6.3	0.7
		117	5.1	0.9
		141	4.7	0.7
16	Abdominal-extremity: perforations of lung, diaphragm, liver, both arms, and back	10	7.2	1.5
		26	7.2	1.3
		38	6.2	1.1
		62	7.2	0.9
		86	6.3	1.0
17	Extremity: compound fracture of mandible and hard pallet; extensive soft tissue wounds of face	38	5.9	1.1
		62	6.5	1.1
		86	6.8	1.0
18	Extremity: massive wound of left thigh; fracture of left femur and perforation of right thigh; high thigh amputation performed	49	6.5	0.4
		73	6.9	0.3
19	Extremity: fracture of right leg and injury to posterior urethra	56	6.6	0.9
		80	7.6	0.9
20	Extremity: large wound of shoulder and pectoral region; fragment in cardiac musculature	12	7.3	1.2
		40	6.8	1.3
		64	6.8	1.2
		88	6.7	1.2
		112	7.1	1.1
		136	7.1	1.1
		160	7.1	1.1
21	Extremity: compound fracture of right tibia and contusion of left leg	4	5.9	1.2
		31	5.7	1.0
		44	5.9	1.0
		68	6.2	0.9
22	Extremity: perforating wounds of left thigh and left arm; large laceration of brachial artery	6	7.4	1.4
		24	6.4	1.1
		48	6.4	1.2
		72	6.5	1.2
23	Extremity: fragment wounds of left thigh, compound fracture of femur; massive muscle damage	3	8.1	1.2
		52	5.9	1.0

TABLE 1.—*Total Protein Values and Albumin-Globulin Ratios for Thirty-Three Patients*—Continued

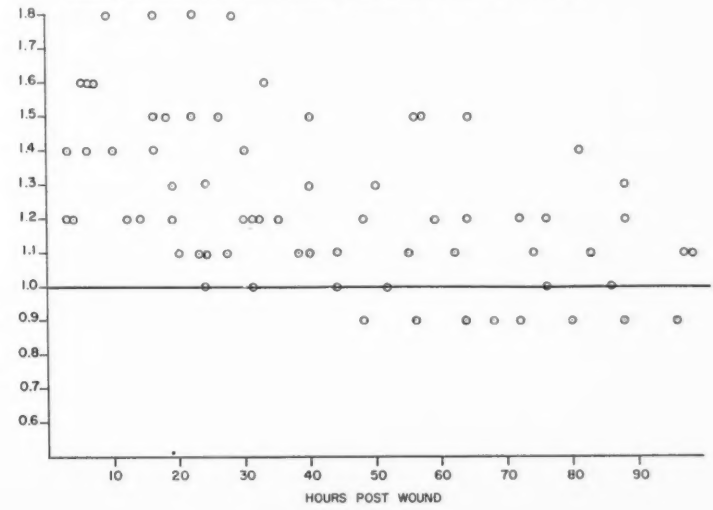
Patient	Wound Description	Time After Wound, Hr.	Total Protein, Gm./100 ml.	Albumin-Globulin Ratio
24	Extremity: compound fracture of left mandible and left arm, perforating wound of left shoulder, right arm, and right leg	16	6.6	1.4
		44	5.8	1.1
		97	6.0	1.1
25	Extremity: traumatic amputation of right foot and ankle, penetrating wounds of right leg, fracture of 3 right fingers	20	5.8	1.1
		23	5.8	1.1
		35	6.2	1.2
		59	6.4	1.2
		83	6.0	1.1
26	Extremity: perforating wound of right shoulder	9	6.8	1.8
		22	5.3	2.0
		28	5.4	1.8
		40	5.3	1.5
		64	5.0	1.5
		88	4.8	1.3
		112	5.0	1.4
		136	5.0	1.4
		160	5.1	1.2
		184	6.3	0.9
27	Extremity: perforating wound of left shoulder, severe compound fracture of the head of humerus	5	7.0	1.6
		16	5.4	1.8
		22	5.2	1.8
		33	5.8	1.6
		57	6.3	1.5
		81	5.8	1.4
		105	6.2	1.2
		129	6.6	1.4
		153	6.2	1.2
		177	6.6	0.7
28	Extremity: traumatic amputation of both legs and penetrating wound of right buttock	3	6.8	1.4
		10	5.5	1.4
		19	6.1	1.2
		31	7.2	1.2
		55	6.6	1.1
		76	6.1	1.0
29	Extremity: traumatic amputation of right hand, multiple wounds of right thigh and compound fracture of right femur	30	6.0	1.4
		40	5.5	1.1
		64	5.7	0.9
		88	5.5	0.9
30	Extremity: compound fracture of left ramus and body of mandible; penetrating wounds of left shoulder, arm and right forearm	7	6.5	1.6
		16	8.0	1.5
		19	6.0	1.3
		22	5.5	1.5
		32	5.3	1.2
31	Extremity: penetrating wounds of both thighs and right arm; laceration of head and face	6	6.1	1.6
		26	6.3	1.5
		56	5.4	1.5
		76	5.8	1.2
		140	5.1	1.2
32	Extremity: penetrating wound of neck; laceration of jugular vein on left side	24	7.5	1.0
		48	8.6	0.9
		72	8.0	0.9
		96	8.2	0.9
33	Extremity: traumatic amputation of left leg at thigh; multiple fragment wounds of right leg and left arm	14	6.2	1.2
		18	6.3	1.5
		24	6.6	1.3
		27	5.8	1.1
		30	5.7	1.2
		50	6.0	1.3
		74	6.6	1.2
		98	6.5	1.1

FIGURE 1.
ALBUMIN-GLOBULIN RATIOS IN 16 COMBAT CASUALTIES WITH ABDOMINAL WOUNDS



closely approximating those obtained by electrophoresis.[6] In general, the procedure consisted in the determination of total protein concentration spectrophotometrically with the biuret reagent and the similar determination of the albumin fraction remaining in solution after flocculation of the globulin with 28% sodium sulfite and a sorbitan ether solution. Conversions are made by comparison with known concentrations of human albumin solution. Because of the empirical nature of the procedure, the technique was performed under rigidly controlled conditions and always by the same investigator. As a check on the proficiency and reproducibility of the technique, a pooled sample of serum was subdivided into 24 small aliquots and stored in the frozen state. With each set of analyses, one ali-

FIGURE 2.
ALBUMIN-GLOBULIN RATIOS IN 17 COMBAT CASUALTIES WITH EXTREMITY WOUNDS



quot of pooled serum was run. In our hands, the average A/G ratio for these analyses on pooled serum was 1.50, with a variation of ±0.06.

After collection and separation of the serum, all samples were stored in the frozen state. Analysis was performed on all samples from the same patient simultaneously. Several samples were preserved with 1:10,000 thimerosal and returned to the Zone of the Interior for complete electrophoretic fractionation.

RESULTS

Table 1 summarizes the serial total protein and albumin-globulin ratio for the 33 patients studied. Patients 1 to 6 and 17 to 25 received dextran preoperatively or postoperatively, and patients 7 to 13 and 26 to 30 received gelatin. The first 16 patients listed sustained abdominal perforations, whereas the latter 17 patients sustained only extremity wounds.

Figures 1 and 2 are scattergrams of the albumin-globulin ratio for the patients with abdominal injuries and those with extremity injuries respectively. Tables 2 and 3 summarize the changes in albumin-globulin ratio following abdominal and extremity injury.

As can be seen from Figures 1 and 2, a progressive decrease in the albumin-globulin ratio occurs with nearly all patients. The degree of the response is noted to be more pronounced with patients sustaining abdominal wounds.

In order to evaluate whether this shift in albumin-globulin ratio was due to a loss of albumin or an increase in globulin, several samples were preserved for electrophoretic analysis. These results are reported in Table 4. These results indicate that there is a decrease in the relative per cent of albumin concurrent with an increase in the relative per cent of α_1 and α_2 globulin. No consistent change in the β and γ globulin levels was noted. This is in agreement with the findings of Hoch-Ligeti [5] in general surgical patients.

TABLE 2.—*Albumin-Globulin Changes in Sixteen Patients with Abdominal Injuries*

	Days After Wound					
	1	2	3	4	5	6
Av. A/G ratio	1.25	1.15	0.93	0.90	0.97	0.90
No. of observations	31	18	15	16	7	5
No. below 1.0	2	3	10	11	4	3
% below 1.0	7	17	67	69	57	60

TABLE 3.—*Albumin-Globulin Changes in Seventeen Patients with Extremity Injuries*

	Days After Wound					
	1	2	3	4	5	6
Av. A/G ratio	1.41	1.27	1.11	1.03	1.20	1.28
No. of observations	25	16	15	14	4	4
No. below 1.0	0	1	5	4	0	0
% below 1.0	0	7	33	29	0	0

TABLE 4.—*Relative Per Cent Protein Fractions per Electrophoresis*

Patient No.	Time After Wound, Hr.	Albumin, %	α_1 %	α_2 %	β %	γ %	Total Protein, Gm./100 Cc.
10	24	57	12	10	11	10	6.0
	39	46	18	14	7	15	5.1
	99	41	25	19	9	6	5.1
30	26	62	15	11	6	6	6.3
	76	47	25	17	6	5	5.8
31	10	59	4	14	6	17	7.2
	62	46	10	21	6	17	7.2

COMMENT

Previous investigators have studied the changes in serum protein after surgery. They have described decreases in albumin-globulin ratio, decrease in albumin and increase in a_1 and a_2 globulin fractions. Our results on 33 seriously injured combat casualties reflect the similar qualitative changes, but quantitatively the changes are more pronounced. Tables 2 and 3 indicate that 67% of the abdominal patients and 33% of the extremity cases possessed serum albumin concentrations which were less than 50% of the total protein on the third postwound day. Similar results were obtained on the fourth postwound day. Previous to this time a progressive decrease in the albumin-globulin ratio had been observed.

Although the quality of the response may be similar for both abdominal and extremity patients, the degree appears more pronounced after abdominal injury. A study of Table 2 and Table 3, however, reveals that the progressive postoperative decrease in albumin-globulin ratio for the two types of wounds is comparable and that the real difference is the result of an early change reflecting itself in the albumin-globulin ratios of the first postwound day. Since the observations made on the first postwound day were generally performed within a few hours after operation, the low albumin-globulin ratios of the abdominal patient suggests that these changes took place before or during operation. Whether there is a specific response to abdominal injury involving localization of albumin in the peritoneal cavity cannot be answered at the present time.

CONCLUSIONS

A serial study of the changes in the serum protein of 33 combat casualties is reported. After abdominal injury there is a rapid decrease in the albumin-globulin ratio of abdominal cases followed by a continued progressive decrease for the next few days. Patients with extremity wounds alone demonstrate a delayed but progressive decrease in the albumin-globulin ratio. Electrophoretic studies reveal the changes to involve primarily a decrease in the relative per cent albumin and an increase in the relative per cent a_1 and a_2 globulin fractions.

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Muscle Metabolism and Catabolism in Combat Casualties

Systemic Response to Injury in Combat Casualties

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It is generally accepted that creatinine produced by endogenous metabolism is derived from muscle creatine and phosphocreatine. The conversion is apparently the result of an irreversible process of normal metabolism which takes place at a constant rate, proportional to muscle mass and independent of muscular exercise.*

The daily urinary excretion of creatinine is constant for the individual, ranging from 1.5 to 2.0 gm. for men and from 0.8 to 1.5 gm. for women. This corresponds to approximately 2% of the total body creatine, from which it is derived. This excretion rate is apparently independent of protein ingestion and is considered an index of muscle metabolism. It is not influenced by exercise or urine volume. Decreased creatinine excretion, with concurrent elevation in plasma level, is generally indicative of impaired renal function, since creatinine is freely filterable at the glomerulus. Decreased excretion in the absence of elevated plasma concentration is usually due to conditions associated with muscular atrophy and paralysis. Increased excretion is associated with increased endogenous muscle metabolism, resulting in the conversion of additional creatine to creatinine.†

Creatine is normally absent from the urine of adult men. Although the total body creatine is approximately 120 gm., 98% is present in muscle tissue. Creatine does not normally appear in the plasma, since its elimination is through creatinine, the waste product of creatine metabolism in muscle. The appearance of creatine in the urine of males is generally associated with wasting diseases, fevers, and certain muscular dystrophies—and thus is an index of catabolism of muscle tissue.

PURPOSE

This study was undertaken to evaluate the response of muscle tissue to direct and indirect injury as part of the total body's systemic response to injury.

Specifically, the study may be subdivided as follows:

(1) The metabolism of muscle tissue—as evidenced by the conversion of creatine to creatinine, following severe wounds with massive muscle damage and with minimal muscle damage.

(2) The catabolism of muscle tissue—as evidenced by release of creatine after similar injuries.

Concurrent with these studies, endogenous creatinine clearance measurements were made to evaluate the glomerular filtration rate of all patients and thereby take into account any effect from renal impairment.

METHODS

Twenty-seven seriously wounded United Nations combat casualties were studied. Heparinized blood samples were drawn from all patients immediately

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* References 1 and 2.

† References 1 and 2.

after the operation and at 12- or 24-hour intervals thereafter. Urine specimens were collected for the same periods by indwelling catheters. All samples of plasma and urine were stored in the frozen state until analyzed.

The determination of creatinine was performed by a modification of the standard method of Bonsnes and Taussky [3] which measures creatinine-like chromogens. In general the procedure was as follows:

A protein-free filtrate of plasma made from 3.0 ml. of plasma by adding 21 ml. water, 3.0 ml. of 10% sodium tungstate, and 3.0 ml. of 0.66 N sulfuric acid. The mixture was filtered after standing for 20 minutes. Duplicate 5.0 ml. aliquots of the filtrate were transferred to colorimeter tubes and 2.5 ml. of a fresh alkaline picrate solution (25 ml. 1% picric acid to 5 ml. 10% NaOH) was added, with shaking. The color which developed was read 20 minutes after the picrate addition at 510 mμ in a spectrophotometer. Urine samples were diluted 1 to 250 and aliquots 2.5 ml. and 5.0 ml. were analyzed by similar technique. A blank standard and a curve were prepared during each series of determinations, with concentrations of 0, 5, 10, 20, and 40γ. Any specimen furnishing an optimal density outside the range of standards was repeated with a more appropriate dilution.

The creatinine clearances were calculated by dividing the creatinine excretion per minute (ml/min. urine flow × mg/ml. creatinine in urine) by the mean plasma concentration during the period of urine collection.

There is no satisfactory method for the direct determination of creatine. However, the conversion of creatine to creatinine by acid, although lacking specificity to a certain degree, is generally used for creatine measurement. Basically, the procedure used was that of Bonsnes and Taussky,[3] which employs the conversion of creatine to creatinine by acid at 20 lb. pressure and measurement of total creatinine before and after hydrolysis. Creatinine was measured by reaction with alkaline picrate and spectrophotometric measurement of the chromogen. The exact procedure for the conversion of creatine to creatinine was as follows: 5 ml. of 1/10 tungstate filtrate of plasma or 5 ml. of 1/250 dilution of urine was placed in covered tubes wtih 1 ml. N HCl and autoclaved for 20 minutes at 20 lb. pressure per square inch. Four ml. of water was added and mixed. Five ml. and 2.5 ml. aliquots were analyzed for total creatinine with 2.5 ml. of alkaline picrate. The chromogen was read at 510 mμ and compared against a standard curve (0 to 40 γ). Equal aliquots of unhydrolyzed samples were measured for preformed creatinine and subtracted from the total. The increase in creatinine content after hydrolysis was converted to creatine by multiplying by 1.16.

The interference of dextran or gelatin with the measurement of creatinine or creatine by the alkaline picrate method was ruled out. Concentrations as high as 3% dextran and 1.5% gelatin did not significantly affect the determination of either creatinine or creatine. Occasionally a cloudiness would develop in the sample, but centrifugation eliminated any spectrophotometric interference.

An empirical classification of casualties was made in relation to degree of muscle damage. Patients who had severe muscle damage were those with major extremity amputation or requiring extensive surgical removal of muscle tissue. Those with minimal muscle damage included less evulsive, penetrating wounds of the extremity. Abdominal perforations were present in both categories.

TABLE 1.—*Twenty-Four-Hour Creatinine Excretion (Gm.) in Casualties with Severe Muscle Damage*

	Postoperative Days						
Patient	1	2	3	4	5	6	7
3	2.9 *	3.0	2.6	...	...	...	...
4	4.0	3.5	2.5	1.7	1.9	2.3	2.1
6	5.7	6.2	2.9	...	...	...	...
11	1.0 *	1.2 *	...	...	...	...	...
12	1.9	2.7	2.9	2.9	2.6	2.7	2.6
13	3.8	3.5	2.3	3.2	...	1.5 *	...
15	2.2 *	2.6	2.3	...	...	...	...
16	4.2	...	...	...	...	...	...
17	2.4	2.3 *	2.6	...	...	...	...
18	3.4	2.9	2.8	...	...	...	...
19	2.1	2.2	2.5	...	...	...	...
20	1.9	1.9	2.2	2.1	1.9	1.9	2.0
21	4.7	3.1	2.6	4.5	4.7	3.1	2.8
23	1.5	1.9	1.8	2.0	2.2	2.4	...
26	...	...	2.6	2.8	2.5	2.4	...
Average	3.2	3.1	2.5	2.7	2.6	2.5	2.4

* Endogenous creatinine clearance below 75 ml. per minute.

RESULTS

1. *Metabolism of Muscle Tissue.*—In order to evaluate the response of muscle tissue to trauma in casualties with direct extensive muscle damage and with minimal muscle damage, the excretion of creatinine in the urine of 27 combat casualties was studied. Since the conversion of creatine to creatinine is believed to be primarily a function of muscle, the excretion rate of creatinine, in the absence of renal impairment, should be an index of muscle metabolism.

Tables 1 and 2 show the 24-hour urinary excretion levels of creatinine for the 27 patients studied. Table 3 shows the average endogenous creatinine clearances for the same patients for the same period. It was noted that every patient showed an increased excretion at one interval or another during the

TABLE 2.—*Twenty-Four-Hour Creatinine Excretion (Gm.) in Casualties with Minimal Muscle Damage*

Patient	Postoperative Days						
	1	2	3	4	5	6	7
1	3.5	3.1	3.9	3.6	2.9	2.9	3.0
2	3.0	2.9	2.6	...	...	...	...
5	3.8	3.1 *	2.5 *	1.0 *	2.9 *	2.1 *	...
7	...	3.5	...	...	...	...	...
8	7.9	4.0	...	...	...	...	...
9	4.9	3.0 *	2.0 *	2.1 *	1.3 *	1.5 *	2.0 *
10	0.7 *	2.8	1.8	...	...	...	...
14	5.1	3.3	2.9	3.2	...	...	...
22	2.5	3.6	3.7	3.5	...	...	...
24	1.1 *	1.6 *	...	...	...	...	...
25	3.0	...	...	...	...	...	...
27	2.5	1.9	1.9	2.1	2.5	...	...
Average	4.0	3.1	2.8	3.1	2.7	...	...

* Endogenous creatinine clearance below 75 ml. per minute.

study (7.9 gm. per day in one patient), but never below normal (1.5 to 2.0 gm. per day) unless accompanied by renal impairment. Moreover, this increased excretion appeared to be independent of the severity of muscle injury. For example, Patients 7, 9, and 10, who sustained penetrating wounds of the abdomen without other involvement, demonstrated increased creatinine excretion as high

TABLE 3.—*Endogenous Creatinine Clearances for Twenty-Seven Combat Casualties*

Patient	Postoperative Days						
	1	2	3	4	5	6	7
1	103	107	139	136	113	108	108
2	107	124	121	...	...	...	...
3	74	86	85	...	...	...	...
4	135	138	102	77	97	116	107
5	79	57	33	12	29	20	...
6	196	200	100	...	...	...	...
7	...	107	...	...	...	...	...
8	285	140	...	...	...	...	...
9	188	70	49	52	35	38	53
10	33	125	82	...	...	...	...
11	40	58	...	...	...	...	...
12	71	109	116	120	116	124	121
13	139	128	80	106	...	55	...
14	207	127	112	126	...	...	...
15	56	80	81	...	...	...	...
16	111	...	...	...	...	...	...
17	77	71	105	...	...	...	...
18	140	117	128	...	...	...	...
19	90	84	140	...	...	...	...
20	82	111	140	121	99	98	109
21	190	113	95	169	178	124	91
22	80	128	135	130	...	...	...
23	...	94	86	98	92	101	...
24	45	65	...	...	...	...	...
25	88	...	...	...	...	...	...
26	...	...	108	121	135	...	...
27	99	90	146	120	97	...	...

TABLE 4.—*Twenty-Four-Hour Creatine Excretion (Gm.) in Casualties with Severe Muscle Damage*

Patient	Postoperative Days						
	1	2	3	4	5	6	7
3	0.1	0.5	0.8	...	...	...	...
4	0.4	1.8	1.9	0.3	0.7	1.2	1.1
15	2.0	3.4	3.3	...	...	...	...
17	1.9	3.8	3.9	...	...	...	...
19	0.3	0.7	0.7	...	...	...	...
20	0.1	0.4	1.0	1.6	2.6	2.7	2.2
23	0.7	0.8	0.9	1.1	1.2	1.2	...
Average	0.8	1.6	1.8	1.0	1.5	1.7	1.7

as 4.9 gm. per day, whereas Patients 15 and 20, who sustained amputations of two extremities, showed only minimal increases in creatinine excretion, 2.6 gm. per day.

Thus it appears that muscle metabolism of creatine to creatinine is increased in all seriously wounded patients and does not appear to be a function of degree of muscle damage.

2. *Catabolism of Muscle Tissue.*—To evaluate the degree of muscle catabolism that might be effected by direct or indirect muscle trauma, urinary creatine excretion rates were studied in 14 of the previously reported casualties. Seven of these had sustained extensive muscle damage, and the other seven, minimal damage. Since creatine does not normally appear in the plasma and urine, excretion was considered an indication of muscle destruction.

Tables 4 and 5 show the 24-hour excretion rates for the patients studied. It was noted that all patients with extensive muscle damage excreted creatine at abnormal rates, as high as 3.9 gm. per day. The patients with minimal muscle damage showed some creatinurea, but it was significantly less in degree.

TABLE 5.—*Twenty-Four-Hour Creatine Excretion (Gm.) in Combat Casualties with Minimal Muscle Damage*

Patient	Postoperative Days						
	1	2	3	4	5	6	7
1	0.1	0.1	0.1	0.1	0.1	0.5	0.5
5	0.2	0.4	1.0	0.6	1.6	1.0	...
7	...	0.1	0.1	...	...	...	...
8	0.1	0.1	...	...	...	...	...
9	1.0	0.1	0.1	0.1	0.1	0.1	0.1
14	0.1	0.3	0.6	0.1	...	...	...
22	0.2	0.7	1.1	0.7	...	...	...
Average	0.3	0.2	0.5	0.3	0.5	0.5	0.3

3. *Endogenous Creatinine Clearance.*—Endogenous creatinine clearance studies were performed at all intervals of urine collection. Samples of urine and plasma were collected at either 12- or 24-hour intervals. Table 3 gives the average clearance values for each 24-hour period. It will be noted that the majority of the patients studied showed adequate clearance rates. Normal clearances have been reported to range from 80 to 108 when corrected to standard body surface.[4]

TABLE 6.—*Plasma Creatinine Levels (Mg. Per Cent) in Twenty-Seven Combat Casualties*

Patient	Postoperative Days							
	0	1	2	3	4	5	6	7
1	2.4	2.4	1.9	2.0	1.9	1.7	2.0	1.9
2	2.6	1.8	1.6	1.5	1.4	...	...	...
3	2.8	2.7	2.5	2.0	1.9	...	...	...
4	2.7	2.0	1.8	1.6	1.8	1.3	1.4	1.4
5	3.0	3.4	4.4	6.2	7.0	7.0	7.4	...
6	1.8	2.0	2.1	2.1	1.7	...	...	...
7	...	3.1	3.6	2.6	2.3	...	...	...
8	2.5	1.9	2.0	...	...	...	...	...
9	2.5	1.9	2.2	2.0	1.9	1.9	1.9	1.9
10	1.4	1.6	1.1	1.6	1.9	...	...	...
11	1.8	1.6	1.4	...	...	...	...	...
12	1.6	1.9	1.8	1.8	1.6	1.6	1.4	1.6
13	1.9	1.9	1.9	2.2	2.0	1.9	1.9	...
14	1.7	1.8	1.8	1.8	1.7	...	...	...
15	3.3	2.3	5.2	1.7	...	...	...	...
16	2.7	2.8	1.9	...	...	...	...	...
17	3.0	2.0	2.0	2.1	1.7	...	...	...
18	2.0	2.2	1.8	1.5	1.3	...	...	...
19	1.9	1.4	1.4	1.2	1.2	...	...	...
20	1.6	1.6	1.7	1.4	1.4	1.4	1.3	1.3
21	1.8	1.6	2.0	2.0	1.8	1.8	1.8	1.6
22	2.5	2.0	2.0	1.8	2.0	1.8	...	...
23	...	1.8	1.9	1.8	1.6	1.8	1.6	...
24	2.1	1.8	1.6	1.7	...	...	...	...
25	3.0	2.1	...	...	...	...	...	...
26	1.9	1.6	1.4	2.2	1.2	1.3	1.2	...
27	1.9	1.5	1.6	1.3	1.4	1.2	...	...

However, a greater spread in normal values results when surface area is not measured, as in the patients herein reported.

Of the 27 patients studied, only four patients (5, 9, 11, and 24) demonstrated any persistent degree of glomerular impairment. Patients 5, 9, and 11 sustained abdominal wounds, and Patient 24 sustained a shoulder wound involving the brachial artery. Nevertheless, these patients improved subsequently and did not require artificial kidney dialysis. Two additional patients (10 and 15) showed decreased creatinine clearance on the first postoperative day but improved markedly thereafter.

Several of the patients (6, 8, 9, 14, and 21) studied showed clearance levels in excess of 150. The abnormally high clearance rate of these patients is reflected by their total creatinine excretion (Tables 1 and 2). This elevated clearance rate may be due to increased tubular excretion, which is an accepted phenomenon.

Table 6 shows the plasma creatinine levels of these patients and provides an additional indication of the kidney efficiency in clearing the plasma of excess creatinine. It was noted that the majority of the patients possessed a high plasma creatinine level. A rapid fall in plasma concentration, however, was observed in all patients except Patient 5.

COMMENT

As the figures in Tables 1 and 2 indicate, increased creatinine excretion occurs with all types of wound. It is impossible to state that such excretion would occur without any muscle damage, since all patients possessed some degree of muscle damage. It is also difficult and not infallible to establish a classification of degree of muscle damage. Because of the empirical nature of the classification, several patients found in one category might more logically belong in the other. However, regardless of the classification, increased creatinine excretion appears to be normal response to injury. And since the formation of creatinine is almost exclusively a function of muscle metabolism, an increase in muscle metabolism appears to follow injury.

The catabolism of muscle tissue, as measured by the excretion of creatine, however, appears to be a function of the degree of muscle damage. It must be noted that the classification according to muscle damage may include other factors contributing to the observed difference in creatine excretion. Perhaps concurrent with extensive muscle damage is an increased residual traumatized tissue which must be reabsorbed and excreted before the healing process can progress. Nevertheless, postoperative muscle catabolism in these patients was significantly greater in the presence of extensive muscle damage.

It should be noted that the loss of creatine, as represented by the combined creatine and creatinine excretion, is in the neighborhood of 25% of the total body creatine in the first seven postoperative days (Patients 1, 4, and 21). The question of whether this profound loss is compensated by increased body synthesis or is an actual depletion in a vital constituent of carbohydrate metabolism must await further investigation.

CONCLUSIONS

An increase in muscle metabolism, as measured by urinary creatinine excretion, was observed in 27 combat casualties. The increase appeared to be independent of type, degree, or location of the injury.

An increase in muscle catabolism, as measured by urinary creatine excretion, was observed in patients sustaining extensive muscle damage. The increase was significantly less in patients with minimal muscle damage.

Endogenous creatinine clearance of these patients reveals impaired glomerular function frequently on the first postoperative day but only occasionally thereafter. Frequently increased creatinine clearances were observed, suggestive of increased tubular excretion.

In general, a systemic response to serious injury, independent of wound site, was observed by an increased metabolism of muscle tissue. A local response in the form of muscle catabolism after extensive muscle injury was also observed.

APPENDIX

WOUND DESCRIPTION

Patient 1: Penetrating wounds of right leg, groin, abdomen, chest, and left arm

Patient 2: Penetrating wounds of scrotum, both legs, hand, and face

Patient 3: Penetrating wounds of abdomen (involving liver and right kidney), right arm, both legs, and buttocks

Patient 4: Penetrating wounds of abdomen, both arms, both legs, pelvis, and buttocks

Patient 5: Penetrating wounds of abdomen, spinal cord, and thigh

Patient 6: Penetrating wounds of the abdomen, buttocks, and left thigh

Patient 7: Penetrating wound of the abdomen (involving stomach, spleen, kidney, and pancreas)

Patient 8: Penetrating wounds of abdomen, right hand and arm, and right flank

Patient 9: Penetrating wound of abdomen

Patient 10: Penetrating wound of abdomen (involving spleen)

Patient 11: Penetrating wounds of abdomen, left leg (amputation), back, left shoulder, right hand, and right leg (compound fracture)

Patient 12: Penetrating wounds of both legs

Patient 13: Penetrating wounds of right foot, ankle, thigh, and left foot (amputation)

Patient 14: Penetrating wounds of right hip and chest

Patient 15: Penetrating wounds of scrotum, left thigh, right leg (amputation), and right forearm (amputation)

Patient 16: Penetrating wounds of left leg (massive) and right ankle (amputation)

Patient 17: Penetrating wounds of left mandible, left arm (fracture), left thigh, left knee, and right forearm

Patient 18: Penetrating wounds of left femur (massive)

Patient 19: Penetrating wounds of right foot (amputation), both legs, and right hand

Patient 20: Penetrating wounds of both legs (amputation) and right buttock

Patient 21: Penetrating wounds of right foot (amputation) and right leg

Patient 22: Penetrating wounds of both legs and left arm (brachial artery)

Patient 23: Penetrating wounds of right foot and ankle (amputation), right thigh, and right hand (fracture)

Patient 24: Penetrating wounds of shoulder and arm (brachial artery)

Patient 25: Penetrating wounds of both legs and left arm and shoulder

Patient 26: Penetrating wounds of right leg (amputation) and left leg

Patient 27: Penetrating wounds of right leg (compound fracture), left leg, left hip, and left hand

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Adrenal Surgery for Psychoses Associated with Cushing's Syndrome

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Psychoses are known to result from alterations in the function of the adrenal. They are found in both the hyperfunctioning (Cushing's syndrome) and the hypofunctioning (Addison's disease) states. Dysfunction of other endocrines may at times be responsible for abnormal mentation; the thyroid was probably the first to be recognized and described.

The case histories of two patients are reported here. They are considered noteworthy because of the prominence and profundity of their psychic disturbances; both had been in institutions for mental disease, and, although both exhibited typical signs and symptoms of Cushing's syndrome, these were not recognized early in the course of the disease.

CASE 1.—A white Syrian woman, aged 33, entered the Brooklyn Hospital Nov. 11, 1947. The following history was obtained chiefly from her husband and mother, as her mental deterioration had progressed to a state where the obtaining of a detailed reliable account was impossible. In her past history, it was noted that she had an early puberty and that menses were always scanty and irregular. Her difficulties had begun (1945) two years before. At the onset she noticed frequent headaches and dizzy spells. She was married shortly thereafter and seemed to adjust well to married life at first. However, about three months after her marriage she became mentally disturbed—she slept poorly and had numerous arguments with her mother, who lived with them. At about this time she began to gain weight rapidly. During 1946, her menstrual periods became irregular, and they stopped altogether by October, 1946. She also became sexually frigid, losing all interest in the opposite sex; her personality showed definite changes; she felt insecure and seemed morbid and depressed. She was seen by a prominent neuropsychiatrist in February and March, 1946. About November, 1946, she began to stay in bed almost constantly; paranoid ideas appeared; she thought people were talking about her and against her and trying to poison her. In August, 1947, she received three electric shock treatments; afterward she complained of pain in the back and lower chest, persisting until her admission. In the few weeks before admission she had been completely confined to bed, was untidy, and expressed suicidal ideas.

Physical Examination.—A woman who appeared much older than her 33 years was seen lying in bed; her body was enormously obese; the extremities were of normal size. A good-sized hump was seen on her back, high between the shoulders, and striae were prominent on her abdomen and breasts. Her face was hairy and severe acne was present. Her hair was oily and unkempt; her skin was dirty and malodorous. Gynecologic consultation revealed no evidence of pelvic pathology. Roentgen examination of skull was reported as being normal. Compression fractures of T8, 10, 11, and 13 were noted; a mild degree of scoliosis was present.

Neurologic Examination.—The report was as follows: There is poverty of speech, paranoid thought, hallucinations, fair orientation, poor insight, and poor judgment.

Mental Status.—When left alone, she lies in bed quietly, and when spoken to, she answers in a whiny high-pitched voice. The context of her speech is childish—she exhibited extreme modesty, to the point of objecting strenuously to physical examination, objecting with childlike crying and protestations.

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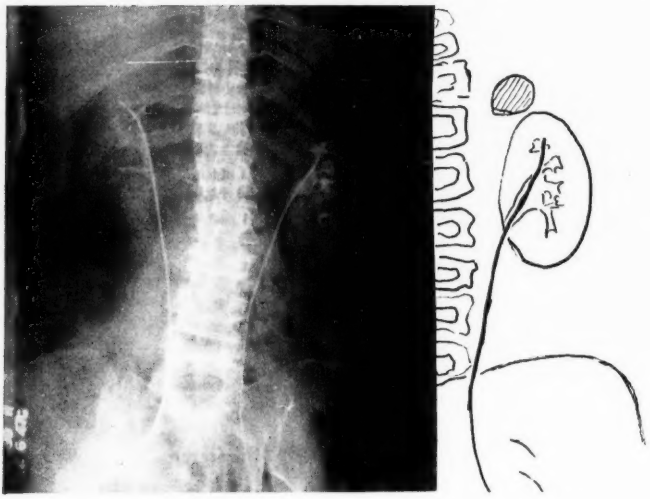


Fig. 1 (Case 1).—Left kidney appears lower than the right. Faint spherical density is seen in the adrenal area.

Pyelography.—Bilateral pyelograms were made. It was noted that both kidneys were normal, but the left side was lower than the right. On one of the films a faint spherical shadow is seen above the kidney in the area of the adrenal (Fig. 1). Perirenal injection of air did not contribute further to its identification—adequate soft tissue shadows were difficult to obtain owing to her enormous obesity.

In short, this woman presented a picture of profound paranoid psychoses with typical findings of Cushing's disease—a shadow suggestive of adrenal tumor was seen lying above the left kidney. 17-Ketosteroid determination was not done.

On Dec. 9, 1947, an adrenal tumor measuring 4×3×2.5 cm. (Fig. 2) attached to a small normal remnant of the adrenal gland was removed.

Our pathologist, Dr. deVeer, reported the tumor as a benign "adenoma of the adrenal cortex." "The remnants of non-neoplastic adrenal tissue are unusual in that the cells are large and foamy. One island of normal medullary tissue is seen. The lumen seems completely encapsulated and is noninvasive."

After removal, no immediate change in blood pressure was noted; two hours later it began to fall, and vigorous supportive measures were required for 36 hours. Convalescence progressed slowly; her nutrition was in a bad state, owing in part at least to her long period of recumbency, and so the wound healed slowly. Further evidence of her poor nutritional state was seen at operation; on removal of the 12th rib, it was found to be demineralized to a marked degree, having a soft, almost cheesy consistency. This process, plus the shock therapy, probably accounted for the compressed fractures of four vertebrae, previously mentioned. She was finally discharged on the 50th day postoperatively, markedly improved.

One year later she was seen on a follow-up visit. The change was dramatic. She had lost the hirsutism and obesity. She was alert and smiling and appeared as a normal attractive woman. Her menses had been resumed; her libido had returned, and on Feb. 15, 1950, she was delivered of a normal boy.

The second patient was less seriously involved mentally when first seen, and the result, while good, has been less striking.

Case 2.—A white married woman, aged 28, believed her difficulty began three years previously. Symptoms were slight at first—increased growth of hair on the face and body, with a slowly developing moon face and obesity of the trunk, the extremities remaining thin; she had not menstruated for two

Fig. 2 (Case 1).—Adrenal tumor (left) bisected operative specimen.

years. Her symptoms had become severer in the past six months; she had become frigid; the obesity increased, and her mental symptoms were aggravated to such an extent a psychiatrist was consulted and she was sent to an institution for mental illness, where she remained for six weeks. She described her feelings as being highly agitated and apprehensive; she felt that she was overwhelmed with an oppressive malady, with little hope of recovery; she required larger doses of sedatives without relief. Although she retained good insight, the mental aspect of her condition was rapidly progressive.

On examination, findings typical for Cushing's disease were found. The skin was hairy and oily and moderate acne was present. Figure 3 illustrates the striae present on the abdomen and breasts. Figure 4 illustrates the Buffalo hump. The tongue was smooth and red, and the corners of the mouth were cracked.

Determinations showed that the urinary 17-ketosteroid excretion was elevated to 26.6 mg.

Perirenal infiltration of oxygen exhibited shadows suggesting small tumor mass on the right side and possibly also on the left.

On Aug. 4, 1953, a bilateral simultaneous exposure of both adrenal areas was made through incisions over the 12th ribs. Both ribs were removed. The right adrenal measured 7 cm. in its greatest dimension and contained an adenoma 3 cm. in diameter, located in its central portion. This side was completely removed. The left gland appeared about twice its normal size but otherwise normal; about four-fifths of this gland was resected. Reports after examination of the microscopic sections are as follows. A benign adenoma of the adrenal cortex was observed on the right. Normal adrenal structures were reported from the left.

The postoperative period progressed smoothly; the blood pressure was maintained with cortisone and an extract of adrenal cortex (Eschatin). On the 12th postoperative day the 17-ketosteroid excretion had returned to normal limits (13.9 mg). She was discharged on the 14th day. Follow-up 11 months later shows marked improvement in her physical appearance; the obesity, striae, moon face, and Buffalo hump have gone. Her nervous symptoms have disappeared; menstruation has returned.

Fig. 3 (Case 2).—Obese abdomen with prominent striae. Female distribution of hair is retained.

Fig. 4 (Case 2).—Moderate "buffalo hump" and moon face.

COMMENT

The symptoms of hyperadrenalism are diverse. The mental aspects of adrenal dysfunction have not been stressed; it is apparent that both these patients had been under observation for their mental symptoms for more than two years without recognition of the adrenal syndrome as an underlying cause. Dysmenorrhea and amenorrhea may also be prominent symptoms.

SUMMARY

Two women with marked psychoses, severe enough to be confined to institutions for mental disease, are reported. The first patient had a profound paranoid psychosis. Both obtained dramatic relief after adrenal surgery. Improvement was slow but constant after operation. About 10 to 12 months were required for complete recovery.

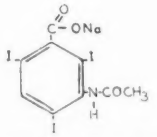
Intravenous Cholecystography with a New Medium

Experience with Sodium Acetnzoate (Urokon Sodium) Seventy Per Cent

THEODORE L. ORLOFF, M.D., Philadelphia

Intravenous cholecystography has not been generally utilized because of fear of severe constitutional reaction. Recently, it has been recognized that, with the refined technique used in preparing iodine solutions for intravenous cholecystography, this former objection is no longer valid. This paper reviews our experience with sodium acetrizoate (Urokon sodium) 70% (developed by the Mallinckrodt Chemical Works) as a cholecystographic agent.

Sodium acetrizoate 70% is a sodium salt of 3-acetylamino-2,4,6-triiodobenzoic acid. It is among the least toxic materials in general use as an intravenous contrast medium. This compound has the following structural formula and contains 65.8% iodine per molecule, or 23.03 gm. of iodine per 50 cc.



Mol Wt 578.9 $C_9H_5NO_3I_3Na$

PREPARATION AND TECHNIQUE

Preliminary catharsis, preferably with castor oil, should be carried out to clear the colon of gas and fecal content. The examination is begun with the patient fasting. One to two cubic centimeters of sodium acetrizoate 70% is injected intravenously, and, if there is no allergic reaction, the injection is completed. Fifty cubic centimeters is injected rapidly (one minute or less) through a No. 18 needle. A preliminary scout film is taken four to eight hours later. Subsequent film studies making use of the recumbent oblique, erect, and lateral decubitus views are utilized.

RESULTS

The intravenous method may be required when doubt concerning the status of gall-bladder function or disease exists following oral cholecystography. If for any reason cholecystography is deemed necessary in the study of the patient with pyloric obstruction or enterocolitis or in those with sensitive stomachs, the intravenous method is indicated.

Gall-bladder visualization with the use of sodium acetrizoate 70% depends upon renal function. The degree of opacity of the cholecystogram is inversely proportional to renal function. The concentration in the gall bladder is best in those patients with diminished renal function. Studies repeated with oral cholecystographic procedures always showed better results. In 26 of 28 cases, gall-bladder visualization was obtained. Satisfactory concentration for diagnosis was noted in 24 out of 28 cases. In one case where there was no visualization of the gall bladder, examination with oral cholecystographic technique gave similar results. The other case of nonvisualization had a serum bilirubin of 1.7 mg. but still was visualized satisfactorily by use of the oral method. The remaining two cases only had fair visualization. There has been no instance of any severe constitutional reaction. Excellent gall-bladder visualization was obtained in one case of a partially obstructing ureteral calculus.

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Department of Radiology, Albert Einstein Medical Center, Northern Division.

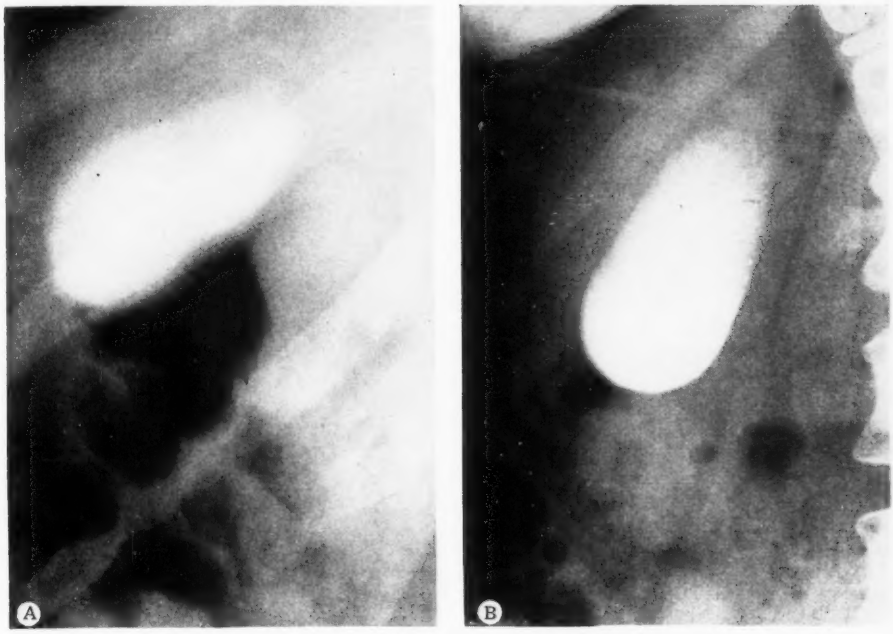
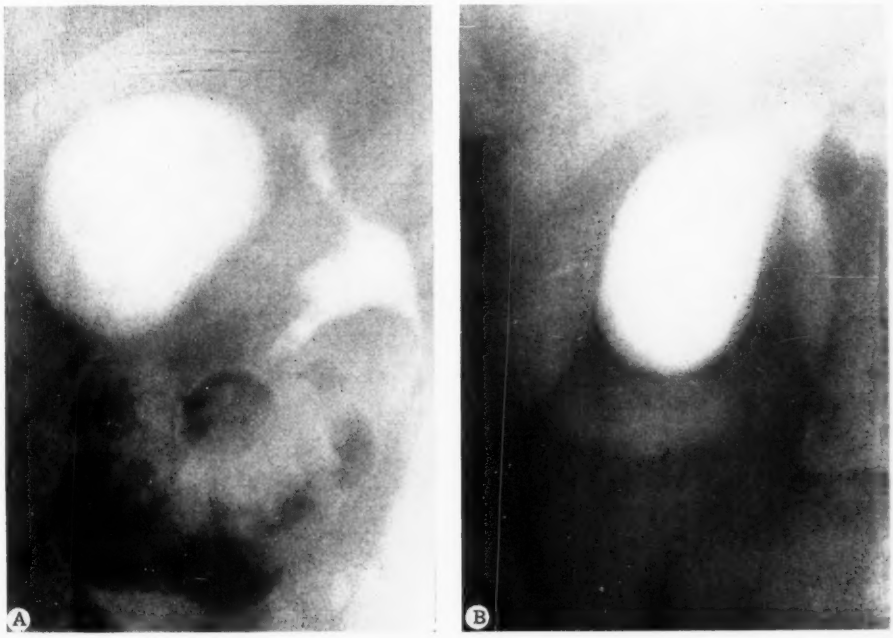


Fig. 1.—Gall-bladder visualization in patient with normal renal function, with use of sodium acetrizoate 70% (*A*) and iopanoic acid (Telepaque) (*B*).

Fig. 2.—Gall-bladder visualization in patient with normal renal function, with use of sodium acetrizoate 70% (*A*) and iopanoic acid (*B*).



SUMMARY

Sodium acetrizoate (Unbroken sodium) 70%, used primarily in intravenous urography, nephrography, translumbar aortography, and angiocardiography can also be used for intravenous cholecystography. The degree of opacity of the cholecystograms is inversely proportional to renal function. The concentration in the gall bladder is best in those patients with diminished renal function. The opacification of the gall bladder in those cases with normal renal function, although sufficient for visualization, is not considered as completely diagnostic as the oral technique, since the proper density is lacking.

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1. Bockus, H. L.: Gastroenterology, Philadelphia, W. B. Saunders Company, 1946, vol. 3, pp. 501-502.

2. Porporis, A. A.: Routine Clinical Experiences Using Urokon Sodium 70% in Intravenous Urography, Radiology **60**:675-86 (May) 1953.

A New Instrument Designed to Retract the Costal Cage in Gastric Surgery

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and
A. SAMPSON, M.D., Pittsburgh

The operation of subtotal gastrectomy has reached a point of excellent execution as far as the technical aspects are concerned. It is generally agreed that in order to obtain a satisfactory result in ulcer one should resect at as high a level as possible technically. Moreover, in total abdominal gastrectomy it is certainly desirable to be able to work with exposure at a high level. This also applies in the operation of subdiaphragmatic vagotomy. In brief, any procedure in the region of the lower esophagus or upper stomach could benefit by better exposure. This is attested to by the fact that some authors have recommended splitting the sternum, while others recommend removal of the xiphoid.

Submitted for publication Dec. 22, 1954.

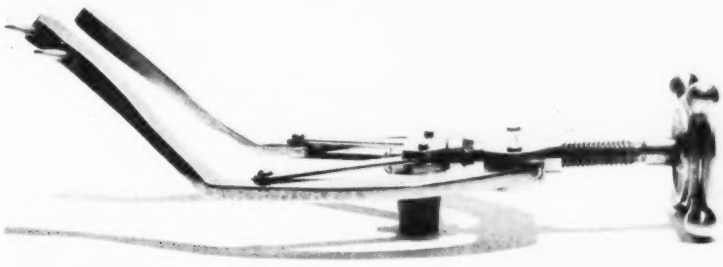
Senior Attending Surgeon (Dr. Rosenburg) and Assistant Surgeon (Dr. Sampson), Montefiore and Homestead Hospitals.

It is generally agreed that the anatomical build of the patient plays a large part in the ability of the surgeon to get exposure for any particular operative procedure. Thus, in gastrectomy the patient with a distinctly narrow angle in the costal margin presents more difficulty than one with a wider angle in the costal cage.

It is in the former type, which incidentally occurs frequently, that this new retractor has its greatest usefulness, because the costal cage comes down acutely on both sides and interferes with manipulation. Particularly is this true when any type of intestinal clamp is used. The need is obviously for some type of self-retaining retractor which will give tremendous spread in the upper angle. One of course is naturally led to the self-retaining chest or laminectomy retractors. These are not satisfactory, because, although they spread, they slide downward toward the lower angle of the cage, inasmuch as they have no grip.

The retractor herein presented was made not only to be powerful but also to grip the

Figure 1.



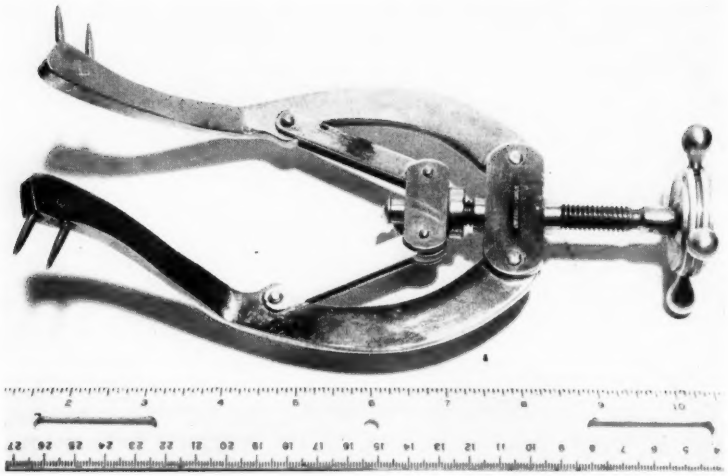
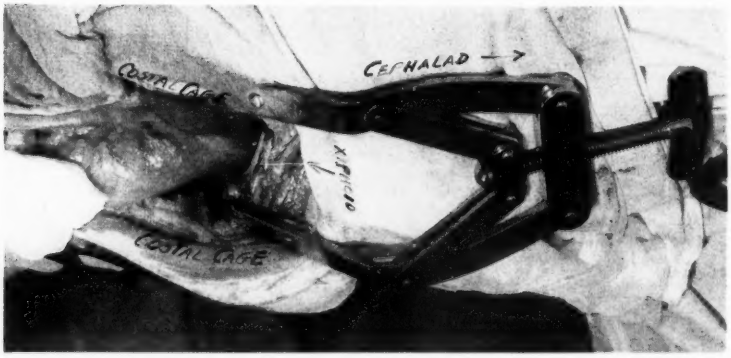


Figure 2.

Figure 3.



costal cage and thus remain in position. The spread is more than adequate, and the spreading mechanism is extremely powerful. The instrument was first made with one spike in each arm, but the subsequent retractor (made by Pilling, Philadelphia) was designed with two spikes on each arm. The retractor spikes may be placed extraperitoneally or intraperitoneally. We find the intraperitoneal position preferable, because all overlying tissue is thus retracted. One might think there could be some aftermath due to the insertion of spikes, but patients have had no complaints that might be related to their presence. In lateral view the retractor is bent at an angle of about 45 degrees, so as to rest on the chest easily when the retractor is in position.

We have used this retractor in about 75 gastrectomies and have found it extremely practical and useful. It has also been found to be of great help in splenectomy. If one decides to combine the use of this spreading retractor with excision of the xiphoid cartilage, the amount of exposure obtained is really amazing and gratifying to the operator.

Miss Lee Schnepp, instrument nurse, and Miss Justine Sykes, operating room supervisor, gave their help in this work.

SURGERY ILLUSTRATED

Intestinal Segments as Internal Pedicle Grafts

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E. J. HILL, M.D.
F. W. PRUST, M.D.
and
R. B. CAMPBELL, M.D., Detroit

THE reinforcement and the replacement of anatomic structures in animals and man has presented a problem of increasing importance with newer and more radical surgical techniques.

Attempts have been made recently to replace structures with metal, plastic, and glass devices. Although these nonfunctional substances are temporarily satisfactory, they deteriorate after a time, set up a foreign-body reaction, or act as foci of infection. We feel that better results might be obtained if viable host tissues could be used.

In addition to the sites where substitutes have been tried, there are many structures in the human body, such as the biliary tract, the urinary bladder, and large defects in the peritoneum, for which there has been no satisfactory means of reinforcement or replacement.

With the hope of improving upon present methods, we are attempting to produce viable functional substitutes for anatomic structures by using intestinal segments as pedicle flaps. These intestinal segments are ideally suited for this purpose because they are anatomically available, they carry a tremendous blood supply, and they can now be sterilized with wide-range antibiotics. The limiting factor in an individual animal is the length of his mesentery, which cannot be determined before laparotomy.

Only long-term observatons can determine whether these intestinal segments will eventually be as useful to the general surgeon as the Gillies skin pedicle graft [1] has been to the plastic surgeon.

Submitted for publication Jan. 20, 1955.

From the Research Department of The Upjohn Company, Kalamazoo, Mich., and the Research Laboratory, Harper Hospital, Detroit.

PROCEDURE

Material.—Segments of jejunum or ileum in dogs.

Preoperative Preparation.—Penicillin, 1,400,000 units intramuscularly, and 0.5 gm. neomycin orally twice a day for 48 hours prior to surgery. 2. Animal starved except for water for 24 hours preoperatively.

Anesthetic.—1. Intravenous pentobarbital (Nembutal) sodium (1 cc. or 50 mg. per 5 lb. body weight). 2. For chest work, intratracheal tube inserted and connected to positive-pressure anesthesia machine, with mixture of air and oxygen being administered.*

Skin Preparation.—1. Abdomen, chest, or both shaved, prepared with tincture of mercocresols (Mercresin), and draped with clean nonsterile towels. 2. Clean nonsterile gloves worn by operators.

Incisions.—Thoracoabdominal incision used to enter thoracic cavity. 2. Midline abdominal incision with extension lateral to penis used to enter peritoneal cavity.

* Mine Gas Respirator, Mine Safety Appliance Co., Pittsburgh.

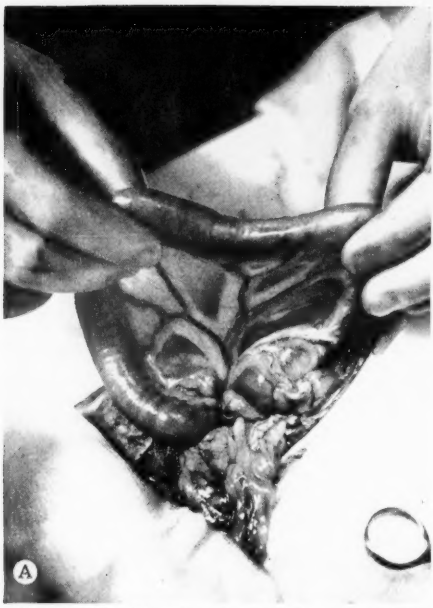


Fig. 13 (*A*).—Selection of proper jejunum or ileum loop.

Fig. 13 (*B*).—The small bowel has been divided at two areas, leaving a central portion of the bowel with its intact blood vessels.

Preparation of Segment.—Segment of bowel to be used selected on basis of being anatomically available to site of defect being repaired. Smaller branches of blood vessels from intestine clamped, divided, and ligated as they are followed through arcuate arteries

Fig. 13 (*C*).—A longitudinal incision has been made, completely opening the isolated loop of bowel. Incision made along the antemesenteric border.

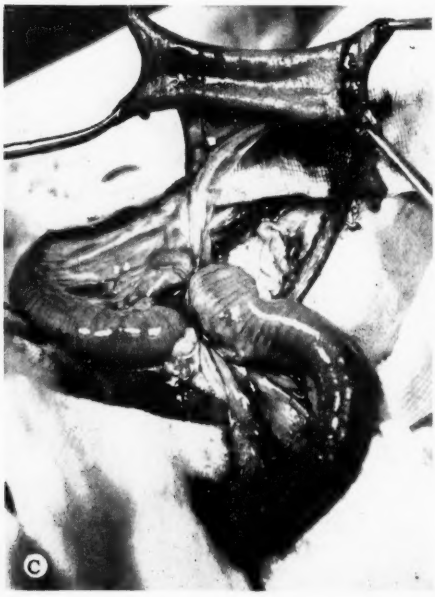
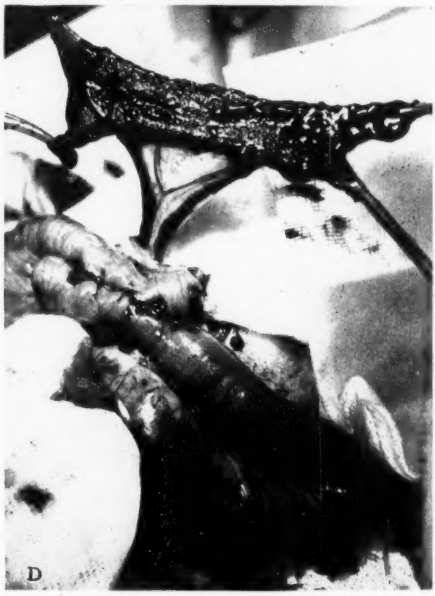


Fig. 13 (*D*).—The mucosal layer of the isolated loop has been removed, leaving the bleeding muscularis layer. Small bowel continuity established by side-to-side anastomosis. This segment of bowel is the pedicle flap ready to be used.



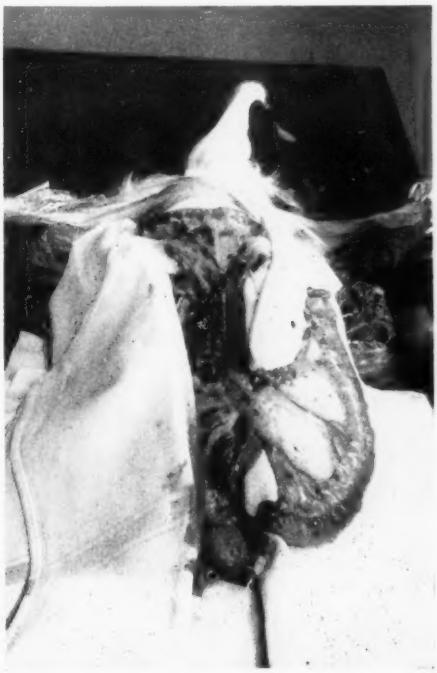
to main branch coming off mesentery. Bowel segment of choice clamped and ligated, and end-to-end or side-to-side anastomosis done, leaving segment completely isolated from rest of intestine, with blood and nerve supply coming directly from mesentery. Segment has very long pedicle, since mesenteric artery and surrounding tissue have been freed up to origin at root of mesentery. With mucous membrane intact, segment can be used as it is for replacing esophagus, biliary structures or lower part of genitourinary system.

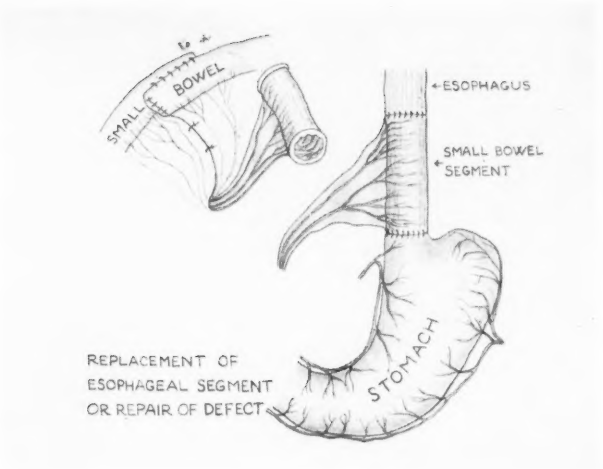
Removal of Mucosa.—If segment is to be used as reinforcing layer around blood vessel transplants, to replace areas of diaphragm, or to repair peritoneum, mucous membrane should be removed. This is easily accomplished with little bleeding by incising segment longitudinally along antimesenteric border, then making incision through mucous membrane and freeing it from surrounding submucosal and muscular layers with dissecting scissors. It can be done with equal ease by infiltrating sterile saline or Ringer's solution between mucosa and muscularis and separating layers by sharp dissection.

Semi-schematic Drawing Showing that the Limiting Factor is the Length of the Small Bowel's Mesentery

APPLICATIONS

These illustrations demonstrate the wide range covered by segments of intestine used as internal pedicle flaps. They can be placed within the thorax as well as within the abdomen.

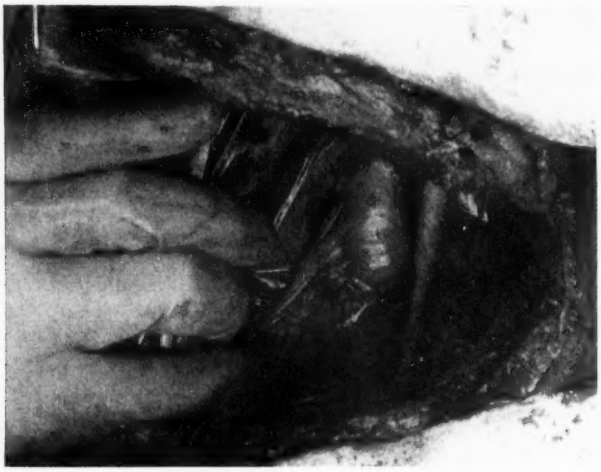


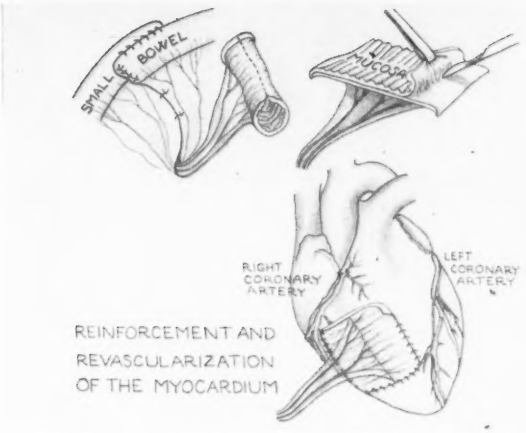


Esophagus

Experimental.—In the thoracic cavity an intestinal segment with its mucous membrane intact can be transplanted into the esophagus to replace an entire segment of the esophagus or to repair a defect.[2] The segment should be inserted in an isoperistaltic manner to avoid dilatation above the insertion. In six animals with the lower third of the esophagus replaced, all are in satisfactory condition after one year.

Clinical Application.—Such a procedure could be of value in cases of esophageal stricture resulting from caustic agents and in cases of resected esophageal varices and of carcinoma.





HEART

Experimental.—We and others[3] have placed an intestinal segment with its mucous membrane removed on an experimentally produced cardiac infarct.

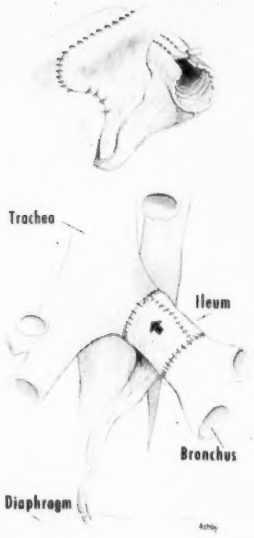
Clinical Application.—While this method is technically feasible, it probably has no advantage over some of the simpler techniques.

Of the numerous attempts to increase the coronary circulation the most effective appears to be Beck's operation,[4] in which the coronary sinus is anastomosed to the systemic circulation. It leaves no doubt that the flow through the coronary veins is reversed.

The talc granuloma technique,[4] the suturing of the omentum[5] or pectoral muscle,[6] and skin grafts † have been advocated to increase the blood supply to the myocardium, but fibrosis occurs in many of these preparations, and there is no increase in coronary circulation. All of these techniques show that vascular anastomosis occurs, but none has demonstrated which way the blood flows in the living animal.

It is doubtful that there is any systemic blood flowing from the grafts to the heart muscle at any time. It has never been proved experimentally. The coronary circulation differs from the systemic circulation in that the coronary blood flow is at its lowest at systole because of the contracted heart muscle, while the systemic blood flow is at its peak. In diastole the coronary circulation is at its peak, while the systemic circulation is at its lowest ebb.

† von Wedel, J., and others: Revascularization of the Heart by Pedicled Skin Graft, read before the Society for Vascular Surgery, San Francisco, June 20, 1954; and Reference 7.



In most animals the mesentery is too short to be brought up to the trachea without undue tension.

Clinical Application.—It is doubtful that this procedure would have a clinical application, although a segment with mucous membrane intact might conceivably be used as a patch in an area of trachea where the tracheal rings remained intact.‡

‡ References 27-30.

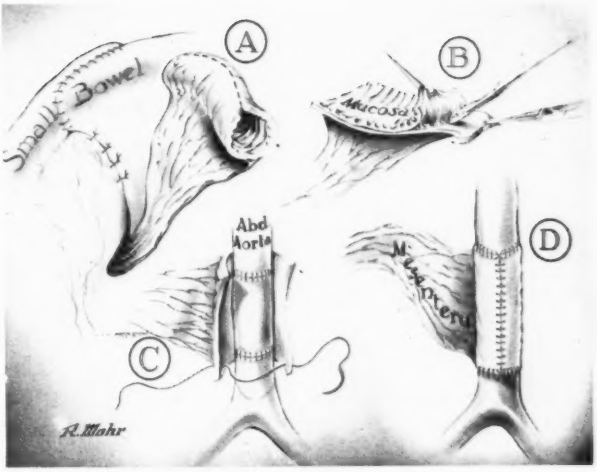
TRACHEA

Experimental.—We have placed a segment of ileum with the mucous membrane intact into the left lower main-stem bronchus and found that it collapses. The animal developed areas of atelectasis, edema, and bronchopneumonia. The lung beyond the inserted segment apparently never functioned.

The replacement of a segment of trachea with intestine was tried in two animals. Both animals died of pneumonia involving the segment of lung distal to the graft.

Experimental. — Successful thoracic and abdominal aortic grafts are being used by many surgeons.[8] We have used both homologous and heterogenous grafts, consisting of dog and human aortas.§ The heterogenous grafts were used in dogs with the assumption that any vessel graft is a nonfunctioning foreign body which is replaced by fibrous tissue. They have proved so far to be as successful as homologous grafts.

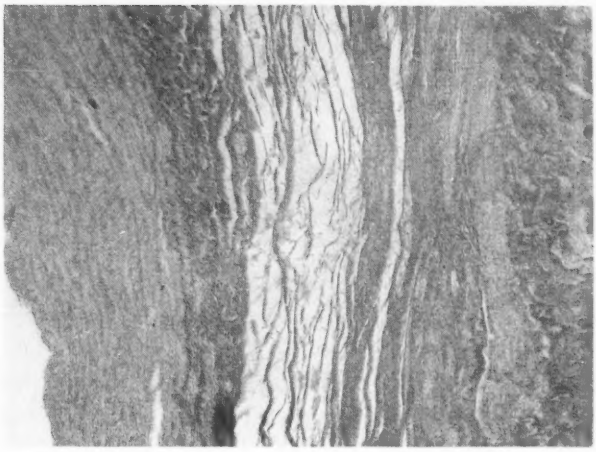
§ References 9-11.

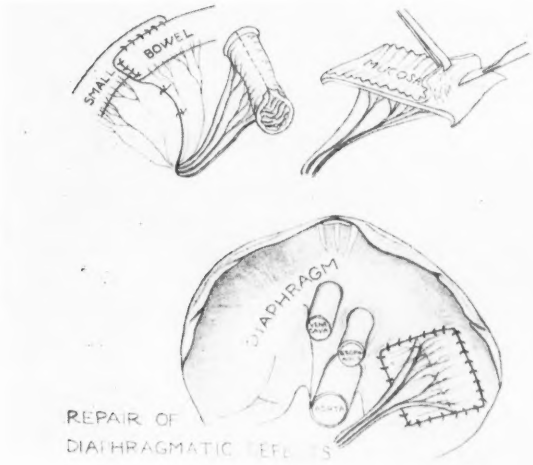


Animals with blood vessels so reconstructed have lived more than four years without aneurysm formation, and the vessels have continued to function. The musculature has remained viable and responds to drug stimulation at laparotomy. The critical observation period of five years has not yet been reached.

The intestinal segment was placed around the blood vessel graft to accommodate it to the continual pounding of pressure and to supply it with a smooth-muscle layer. Since only the musculature was desired for this purpose, the mucous membrane was removed before the intestinal segment was trimmed to the desired size. It was placed about the graft and extended approximately 1 cm. beyond the suture lines at each end.

Clinical Application. — One of the major problems of blood vessel grafts is their dilatation and the formation of aneurysms. This may be prevented if the graft can be reinforced with a smooth muscle layer. The microscopic section shows fibrosis with no infection between aorta and intestinal reinforcement.

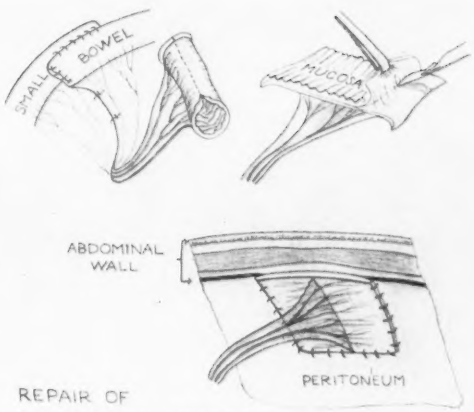




Clinical Application. — The repair of diaphragmatic defects is sometimes complicated by the lack of sufficient tissue to close the defect, particularly in children with developmental defects of the abdominal wall. The technical ease with which intestinal segments can be placed at the desired site overcomes this difficulty.

DIAPHRAGM

Experimental.—Segments of intestine with the mucosa removed and the blood supply intact are easily swung up to repair diaphragmatic defects. These grafts cover the defect, separate the thoracic and peritoneal cavities, and supply a peritoneal surface on the abdominal side.[12]

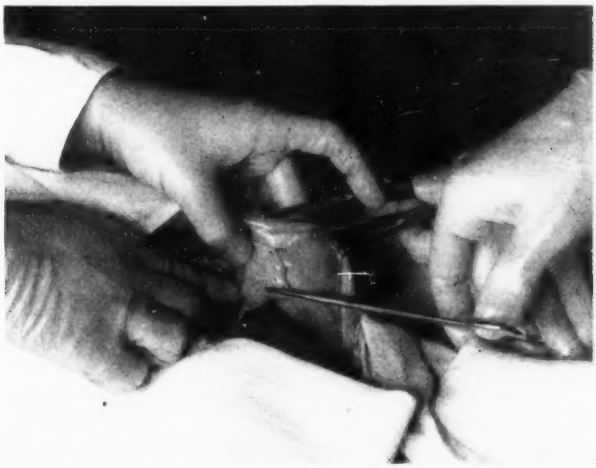


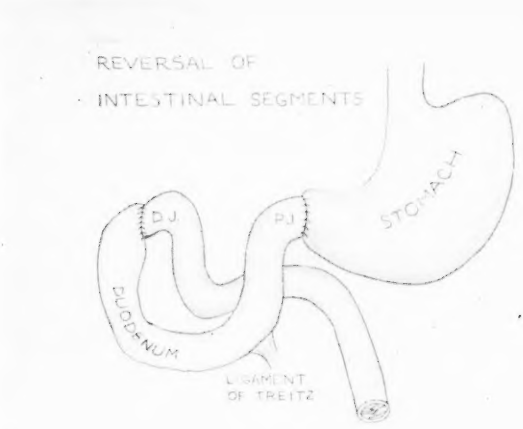
REPAIR OF PERITONEAL DEFECTS

PERITONEUM

Experimental.—Peritoneal defects have been repaired by use of intestinal grafts with the mucous membrane removed. In animals these grafts were observed to work better posteriorly and laterally than anteriorly. However, if used to repair an anterior abdominal wall defect, they could act like a Meckel's diverticulum attached to the abdominal wall. It must be remembered that loops of bowel can be caught around this stringlike mesentery, which contains blood vessels, and an intestinal obstruction could occur. This hazard can be eliminated by cutting the mesentery at a later date, after the graft has "taken."[12] Skin can be grafted directly on to the intestinal segment.

Clinical Application.—Developmental defects in children often necessitate peritoneal repair. Intestinal segments can be used as a source of material for making such repairs.

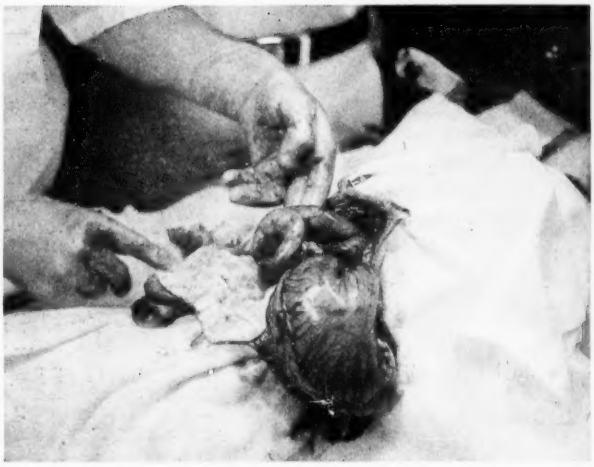




side anastomosis produced blind pouches which gradually filled up with wood shavings from the dogs' cages and led to intestinal obstruction after several months. An oblique anastomosis eliminated these difficulties an proved to be a satisfactory method in our hands. In 70% of the animals, jejunal ulcers developed within six months of the operation. If this method of antiperistaltic anastomosis were used in man when a segment of bowel was replaced or when segments were reanastomosed, the peristaltic waves would work against each other to form a physiologic obstruction, with

Reversed Segments

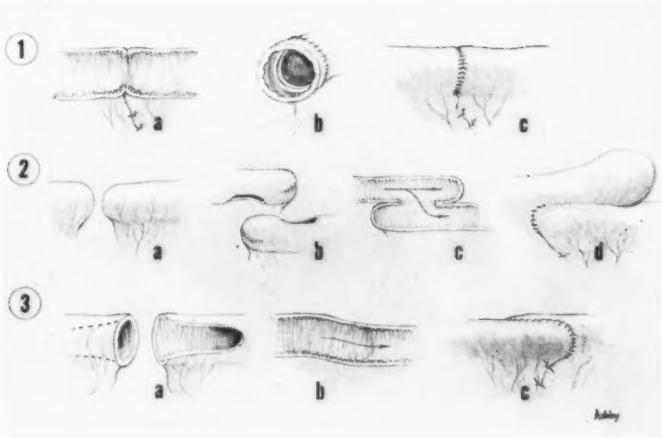
Experimental.—We have previously reported the production of experimental ulcers by reversing the duodenum.‖ The distal end of the duodenum is anastomosed to the antrum of the stomach, and the proximal duodenum in the pyloric region is anastomosed to the proximal jejunum, producing a physiologic obstruction and hypersecretion of hydrochloric acid. An end-to-end anastomosis produced a high intestinal obstruction. The animals in this series all died in the early postoperative period. The side-to-



‖ References 14 and 15.

dilatation of the bowel above the anastomosis and a marked delay in emptying time of the intestine.

Clinical Application. — Van Prohaska [16] has pointed out that in subtotal gastric resections there was a higher percentage of complications (belching, gastric dilatation, delayed emptying time) in patients with antiperistaltic gastrojejunostomies than in a similar series in which the gastrojejunostomy was isoperistaltic. These clinical results can be explained by the results achieved in reversing the duodenum. An experimental application of the reversed segment is included here.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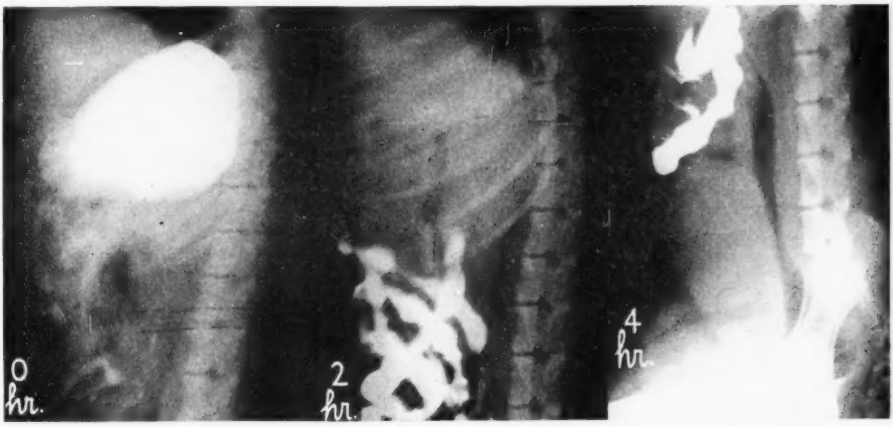
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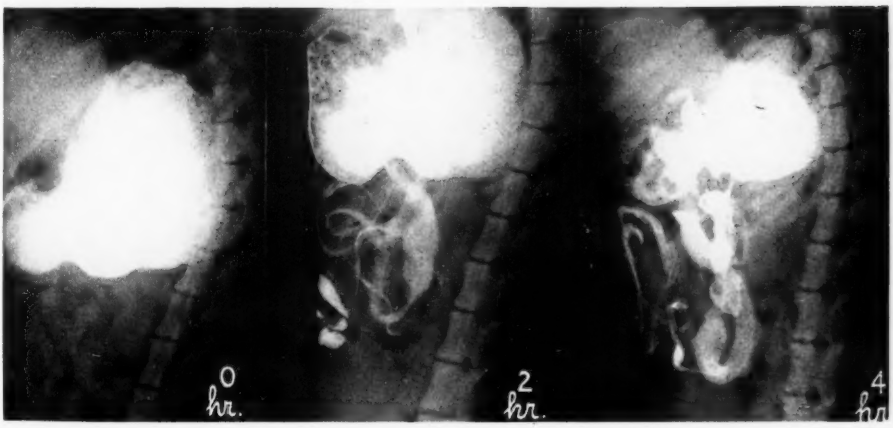
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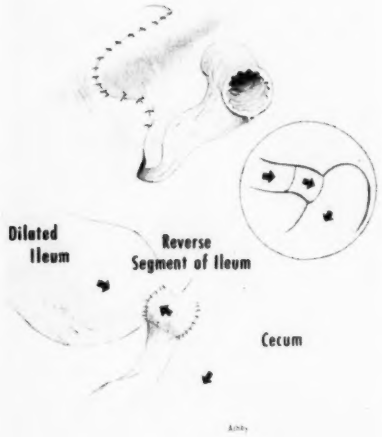


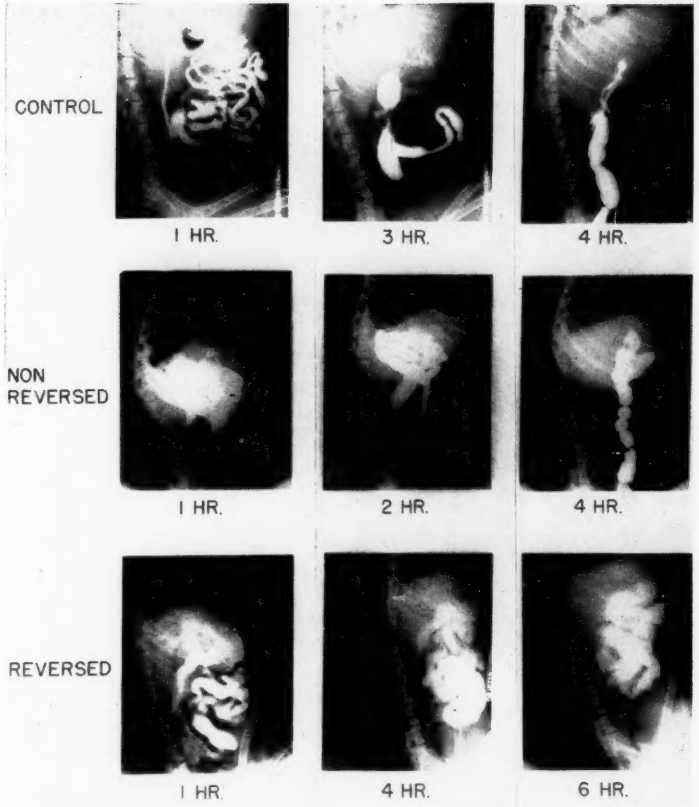
Removal of Three-Quarters of Small Bowel

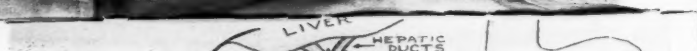
Experimental.—It has been established that animals can maintain themselves on an ordinary laboratory diet if two-thirds of the small bowel is removed but that they die when three-quarters of the small bowel is removed.

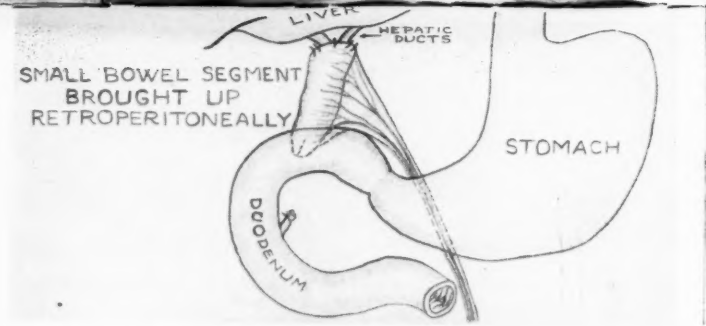
In a series of three animals 75% of the small bowel was removed. They lost weight and died of cachexia within three months.

In a second series of three animals 75% of the small bowel was removed, from the ileocecal junction to the jejunum, leaving 25% of the length of bowel, from the ligament of Treitz to the ileocecal junction. Approximately 1 in. of the remaining small bowel was transected, reversed, and reanastomosed so as to function in an isoperistaltic manner. These animals showed a delayed emptying time and maintained weight.

Clinical Application. — This procedure of reversed segment may be of use in cases of mesenteric thrombosis where a large percentage of the small bowel has been removed.



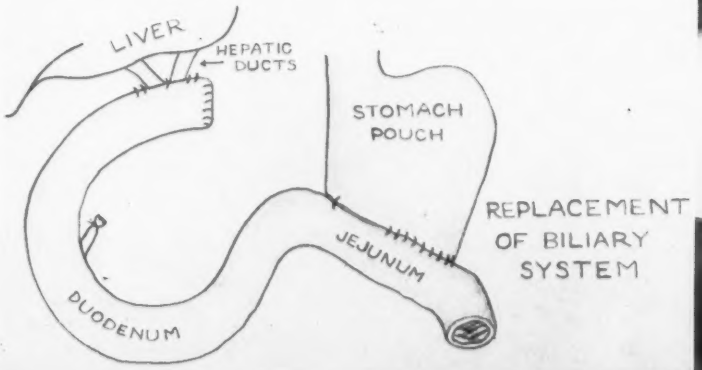


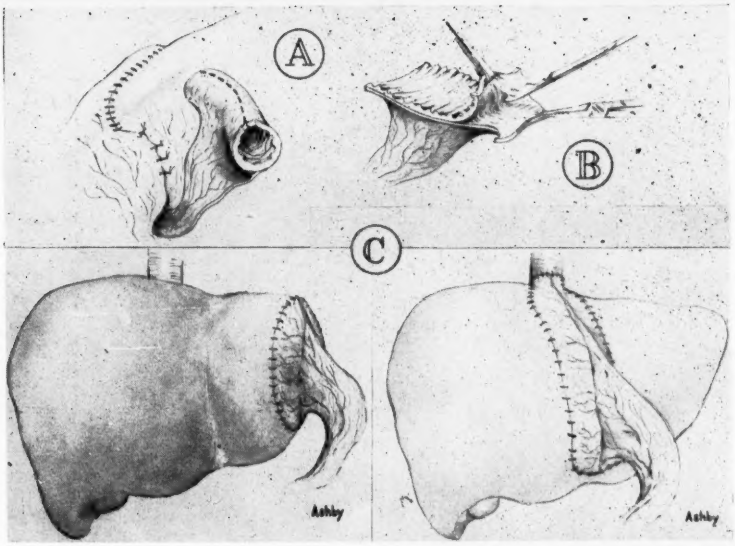


Biliary System

Experimental.—In the biliary system the gall bladder, the hepatic ducts, and the common duct are removed, the stubs of the hepatic ducts being left long enough to identify them at the hilum of the liver. A segment of the intestine is brought out retroperitoneally behind the duodenum or the stomach in such a manner that the peristalsis of the intestinal segment is away from the liver. The segment is sutured to the hilar area with a one-layer technique, surrounding the ducts, and the distal end is brought down to the duodenum. At the distal end a cone is formed by removing a wedge from the antimesenteric border and doing an end-to-side anastomosis between the segment and the duodenum. This forms a dilated biliary system which carries bile into the duodenum by the peristaltic action of the intestine. Since this system has its own blood supply, it will not slough. An end-to-side anastomosis into the duodenum is done to prevent the formation of blind pouches, which would act as reservoirs for particles of food. The peristalsis in the transplant is away from the hilum of the liver, tending to force bile into the duodenum and preventing the duodenal contents from obstructing the biliary flow, as can happen when the jejunum is anastomosed directly to the ducts of the biliary system.

Clinical Application.—A variation of this procedure has been used successfully in three humans. After the hepatic duct remnant is dissected out, the duodenum is transected at the pylorus and the end is inverted. The duodenum is anastomosed to the common-duct remnant. A subtotal gastrectomy is done, using an anterior Polya-Hoffmeister type of gastrojejunostomy. This allows bile to drain into the duodenum, preventing stomal ulcer formation. The gastrojejunostomy keeps food from entering the area, with subsequent plugging of the hepatic radicles.[13]





LIVER

Experimental.—An intestinal segment with its mucous membrane removed has been used to peritonealize a raw surface of the liver in the dog after the removal of one or several lobes. The active bleeding from the cut surface of the liver was controlled with a running through-and-through stitch, and the intestinal segment was sutured over the raw area. These intestinal segments are

capable of carrying as much arterial blood to the liver as the hepatic artery.

An attempt has been made to produce a mesenteric superior caval shunt by suturing the intestinal segment to the liver after a strip of capsule is removed up to the superior vena cava. As yet no injection studies have been done on these animals to see if arteriovenous fistulae, rather than venous shunts, are being produced. Clinically, the animals have not developed symptoms of arteriovenous fistulae. An abundant anastomosis develops between the intestinal segment and either the denuded or the serosal surface.

Clinical Application.—This might be of value as another shunt technique to reduce portal hypertension.¶

¶ References 23-26.

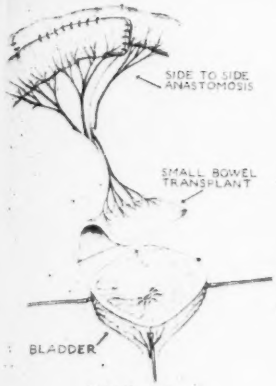


FIGURE A

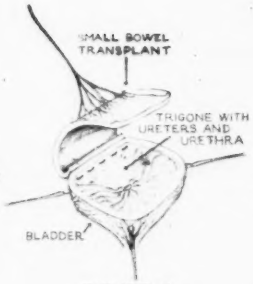


FIGURE B

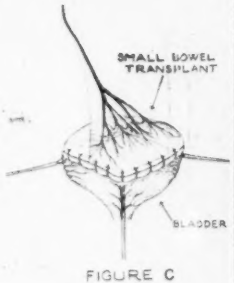
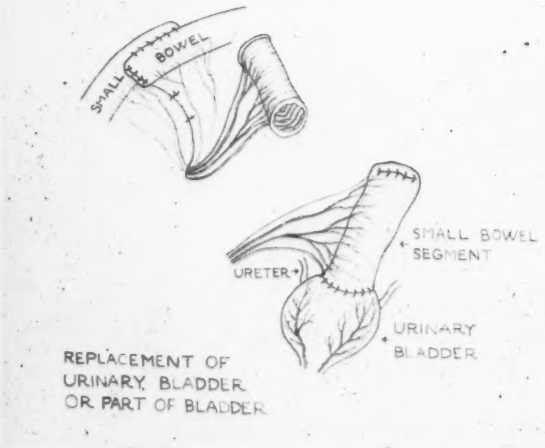


FIGURE C



URINARY BLADDER

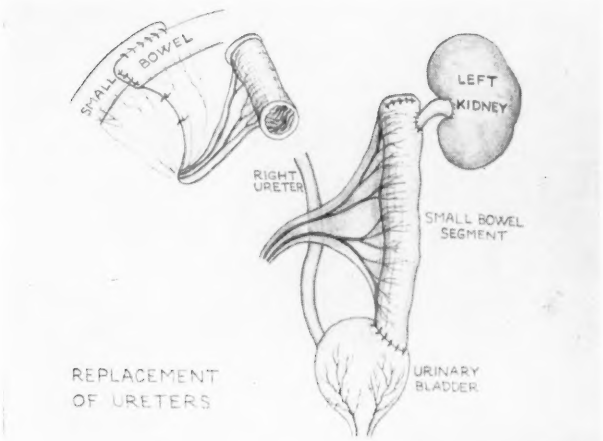
Experimental.—When the urinary bladder is replaced with intestinal segments, the mucous membrane may or may not be removed. The entire urinary bladder was replaced down to the trigone in eight animals. In such cases the segment of intestine must be made long enough to hold the same volume of urine that the full bladder would normally hold.[17]

Several of our animals have gone one year with no difficulty in passing urine, the bladders emptying only once or twice a day. Pyelograms and blood chemistry studies on these animals are normal. Urine cultures are negative.

At laparotomy it was observed that the bowel segment acts as a safety valve, since the bladder hypertrophies up above the trigone and in several months is nearly as large as the original bladder.# The intestinal mucosa apparently reverts to a more primitive type, undergoing a mucoid type of degeneration. Calculi formed when nonabsorbable surgical (silk) sutures were used on the inner layers.

Clinical Application.—This method is already in use by numerous investigators.

References 18 and 19.



Bladder and Ureters

Experimental.—The urinary bladder and one ureter may be replaced by using the same technique as for the bladder. In dogs this is technically easier than replacing the bladder alone.

As yet we have not replaced both ureters and the urinary bladder.*

Clinical Application.— Such a procedure could be valuable in handling various types of tumors.

* References 20-22.

The Use of Viable Intestinal Segments as Internal Pedicle Homografts

Site of Transplant	Mucous Membrane	No. of Animals	No. and Cuases of Postoperative Deaths	Percent Mortality	Postoperative Complications	Results in Animals	Present Methods	Theoretical Human Application	Practical Human Application
Esophagus	Intact	3	0	0	1 Pleuritis	Satisfactory	Plastic tubes; jejunum, stomach or bowel transplanted into chest	Replacement of esophageal segment or defect	See reference 2
Heart	Removed	3	1 Purulent pericarditis	33	2 Adhesive pericarditis	Satisfactory	Talc granulomas, omentum, skin, Beck's operation, pectoral muscle	Production of coronary collaterals	See references 3, 4, 5, 6, 7
Bronchus	Intact	3	3	100	Atelectasis Pneumonia	Unsatisfactory	None	None	See reference 26
Aorta	Removed	32	8 Abscesses 2 Anesthetic	31	7 Infections ? Occlusion of grafts	Satisfactory	Wiring, cellophane, dicetyl phosphate, artery graft	Reconstruction functioning aorta with a muscularis	See references 8, 9, 10, 11
Diaphragm	Removed	3	0	0	1 Pleural effusions	Satisfactory	Fascia lata, tantalum mesh	Closure of diaphragmatic defects	See reference 12
Peritoneum	Removed	3	0	0	1 Wound infection	Satisfactory	Plastic gauze, tantalum mesh	Repair of peritoneal defects	See reference 12
Reversed Duodenal Segments	Intact	18	8 Obstruction	44	70% of 10 survivors developed ulcers in 5-1/2 months; all had dilated atonic stomachs, duodenums and biliary systems.	Ulcers produced in 70% of animals	----	Antiperistaltic anastomoses not done intentionally	See references 14, 15, 16
Biliary System	Intact	3	1 Bile peritonitis	33	0 (Early)	Satisfactory	Polyethylene tubes, choledochoduodenostomy or jejunostomy, veins	Replacement of biliary system	Repair of common duct (3 cases done by authors) See reference 13
Liver	Intact	4	0	0	0 (Early)	Satisfactory	Porto-caval or spleno-renal shunts	Supply more blood to liver? producing a mesenteric superior caval shunt in portal hypertension	See references 23, 24, 25
Urinary Bladder	Intact	10	2 Anesthetic	20	3 Urinary infection All had atonic bladders	Satisfactory	Ureterostomy to skin or sigmoid	Replacement of urinary bladder	See references 17, 18
Ureter	Intact	2	0	0	1 Pyuria	Satisfactory	Ureterostomy to skin or bowel	Replacement of ureter	See references 19, 20, 21

CONCLUSIONS

Viable intestinal segments can be used as internal pedicle flaps to replace or reinforce various structures in the thorax and the abdomen.

Drs. W. W. Allen, E. E. Beals, K. E. Corrigan, L. R. Dragstedt, N. A. Drake, F. D. Dodrill, R. E Erickson, R. L. Johnston, I. A. Pearson, H. S. Saltzstein, A. Tazelaar, E. G. Upjohn, W. Veldkamp, and F. E. Visscher assisted in this work, which was begun in 1946.

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